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## SOME EXAMPLES OF THE USE OF THE t-TEST ON PHYSIOLOGICAL DATA.

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IN this article I wish to illustrate the arithmetic involved in applying the *t*-test to data obtained in physiology and related branches of experimental medicine. The main purpose is to provide a set of worked examples based on data that have some intrinsic interest to the physiologist; but an attempt has also been made to discuss in a non-technical way some theoretical points that arise in the interpretation of these data. Anyone who has occasion to use the *t*-test frequently will find it helpful to study the theoretical aspects much more fully than is attempted here.

The test is used in dealing with a statistical problem which is quite common in experimental physiology, and which may be described in a general way as the problem of deciding whether two groups differ in respect of some particular measurement; or, in other cases, the problem of whether a group examined under one set of conditions differs in some measurement from the same group examined under a different set of conditions. The two groups may often be appropriately called "control" and "experimental". An important feature of the test is that it can be applied to experiments in which the number of cases is necessarily small, and this may have encouraged people to refer to the test as Fisher's *t*-test, since R. A. Fisher has made such important contributions to the statistical theory of small samples. It is true that Fisher has played a part in developing the *t*-test, but his main contribution has been that of verifying, and extending, and making known the work of W. S. Gosset, who, writing under the pseudonym of "Student" (1908), first published the basic theory of the method and some of its applications. Perhaps a reasonable nomenclature is to speak of "Student's" test when one is considering paired observations and to refer to Fisher's modification when the observations are not paired. It may even be an advantage to use different names for these two varieties of the *t*-test, for, as will be shown later, they have been confused in practice.

### Calculation of the Mean, the Standard Deviation and the Standard Error of the Mean of a Series of Results.

The calculation of the mean of a series of results and the standard error of the mean are necessary parts of the test, and are therefore illustrated by a preliminary example given in Table I. The data consist of a series of 32 measurements of the systolic blood pressure made by Kossmann (1946) on healthy males. The mean may be calculated by summing the measurements and dividing by 32; but it is sometimes more convenient to express the measurements as deviations, positive or negative, from some arbitrary figure, and then to obtain the mean by adding the average of the deviations to the arbitrary figure. The arbitrary figure is chosen to make the deviations conveniently small; for instance, 120 is used in the example given. The use of both methods is illustrated in Table I, and the same answer, 121·7, is obtained in each case.

The first step in the calculation of the standard deviation is to evaluate the sum of the squares of the deviations from the mean. The straightforward way to do this is to subtract the mean, 121·7, from each observation, square the answers, and then sum the squares. This gives the result 4761·28 shown at the foot of the fourth column. It

is often referred to briefly as "the sum of the squares". This method of calculation of the sum of the squares is not often used, because, as in the case illustrated, the mean is not usually an integer and the squaring of the deviations from the mean is laborious. The correct answer can be obtained by either of two simpler methods. In the first, one begins by subtracting from the original observations, not the correct mean, but some convenient number which will leave small deviations. In the example, 120 is the number chosen. The deviations −15, −2, and so on, are then squared and the squares are summed to give the answer 4849. This answer must be corrected for the fact that the deviations were not measured from the mean. The correction to be subtracted is found as follows: the sum of the deviations, namely 53, is squared and the square is divided by the number of cases. When this correction is applied, the answer obtained, as shown at the foot of Table I, is 4761·22. This is slightly more accurate than the first answer of 4761·28, for this latter involves the use of the mean, which was accurate to the first decimal place only.

TABLE I.

*The Systolic Blood Pressure of 32 Healthy Young Males. Calculation of Mean, Standard Deviation, and Standard Error of Mean.*
(Data from Kossmann, 1946.)[1]

| Systolic Blood Pressure. (Millimetres of Mercury.) ($X$.) | $X-120$. | $X-121\cdot7$. | $(X-121\cdot7)^2$. | $(X-120)^2$. | $X^2$. |
|---|---|---|---|---|---|
| 105 | −15 | −16·7 | 278·89 | 225 | 11,025 |
| 118 | −2 | −3·7 | 13·69 | 4 | 13,924 |
| 114 | −6 | −7·7 | 59·29 | 36 | 12,996 |
| 116 | −4 | −5·7 | 32·49 | 16 | 13,456 |
| 120 | 0 | −1·7 | 2·89 | 0 | 14,400 |
| 122 | 2 | 0·3 | 0·09 | 4 | 14,884 |
| 122 | 2 | 0·3 | 0·09 | 4 | 14,884 |
| 110 | −10 | −11·7 | 136·89 | 100 | 12,100 |
| 120 | 0 | −1·7 | 2·89 | 0 | 14,400 |
| 104 | −16 | −17·7 | 313·29 | 256 | 10,816 |
| 112 | −8 | −9·7 | 94·09 | 64 | 12,544 |
| 144 | 24 | 22·3 | 497·29 | 576 | 20,736 |
| 118 | −2 | −3·7 | 13·9 | 4 | 13,924 |
| 142 | 22 | 20·3 | 412·09 | 484 | 20,164 |
| 128 | 8 | 6·3 | 39·69 | 64 | 16,384 |
| 140 | 20 | 18·3 | 334·89 | 400 | 19,600 |
| 128 | 8 | 6·3 | 39·69 | 64 | 16,384 |
| 132 | 12 | 10·3 | 106·09 | 144 | 17,424 |
| 120 | 0 | −1·7 | 2·89 | 0 | 14,400 |
| 146 | 26 | 24·3 | 590·49 | 676 | 21,216 |
| 116 | −4 | −5·7 | 32·49 | 16 | 13,456 |
| 122 | 2 | 0·3 | 0·09 | 4 | 14,884 |
| 108 | −12 | −13·7 | 187·69 | 144 | 11,664 |
| 124 | 4 | 2·3 | 5·29 | 16 | 15,376 |
| 98 | −22 | −23·7 | 561·69 | 484 | 9,614 |
| 120 | 0 | −1·7 | 2·89 | 0 | 14,400 |
| 120 | 0 | −1·7 | 2·89 | 0 | 14,400 |
| 124 | 4 | 2·3 | 5·29 | 16 | 15,376 |
| 120 | 0 | −1·7 | 2·89 | 0 | 14,400 |
| 122 | 2 | 0·3 | 0·09 | 4 | 14,884 |
| 108 | −12 | −13·7 | 187·69 | 144 | 11,664 |
| 150 | 30 | 28·3 | 800·89 | 900 | 22,500 |
| Totals 3,893 | 53 | — | 4761·28 | 4,849 | 478,369 |

[1] (i) Calculation of mean:

$$\text{First method, mean} = \frac{3893}{32} = 121\cdot7.$$

$$\text{Second method, mean} = 120 + \frac{53}{32} = 120 + 1\cdot7 = 121\cdot7.$$

(ii) Calculation of sum of squares of deviations from the mean:
First method, sum of squares = 4761·28.

$$\text{Second method, sum of squares} = 4849 - \frac{53^2}{32} = 4849 - 87\cdot78 = 4761\cdot22.$$

$$\text{Third method, sum of squares} = 478{,}369 - \frac{3893^2}{32} = 478{,}369 - 473607\cdot78 = 4761\cdot22.$$

(iii) Calculation of standard deviation of series and standard error of mean:

$$\text{Variance of series} = \frac{4761\cdot22}{31} = 153\cdot59.$$

$$\text{Standard deviation of series} = \sqrt{153\cdot59} = 12\cdot4.$$

$$\text{Variance of mean} = \frac{153\cdot59}{32} = 4\cdot800.$$

$$\text{Standard error of mean} = \sqrt{4\cdot800} = 2\cdot19.$$

The second simple method is a modification of that just given. Zero is subtracted from the observations before squaring; in other words, the figures are squared as they stand, and the sum of these squares amounts to 478,369. The correction to be subtracted is then given by the following rule: square the total of the observations, namely 3893, and divide by the number of cases. The correction is then 473,607·78 and the sum of squares, as before, is 4761·22.

To obtain the variance of the series, one divides the sum of squares by one less than the number of observations. The term "degrees of freedom" is used for this divisor, a partial explanation of the name being that if one nominates the mean and all but one of the original observations of a series, one has, in effect, described the whole series; in this sense there is no freedom as to what the final observation will be, and the degrees of freedom are then one less than the number of observations. The standard deviation is obtained from the variance by extracting the square root. In the example given there are 31 degrees of freedom, so that to obtain the variance of the series one divides 4761·22 by 31. The answer is 153·59, and the square root of this, namely 12·4, is the standard deviation of the series.

The mean of a series of blood pressures or other measurements made in an experiment can be thought of as one of a whole population of possible mean values which could be obtained by indefinite repetition of the experiment. The mean would vary somewhat from experiment to experiment, and it can be shown that the variance of the mean is $\frac{1}{n}$ times the variance of the series, where $n$ is the number of cases. The square root of the variance of the mean is the standard deviation of the mean, or, as it is usually called, the standard error of the mean. In accordance with these rules the variance of the mean of the blood pressures is 153·59 divided by 32. This gives 4·800, and hence the standard error of the mean is the square root of 4·800, that is, 2·19.

### The Normal Distribution.

Another introductory idea needed for a description of the *t*-test is the idea of a normal frequency distribution. If we draw a graph in which, say, systolic blood pressure is represented along the $x$ axis and the number of men having the various systolic pressures is represented along the $y$ axis, we have the graph of a frequency distribution. The normal distribution represented in this way is a continuous, symmetrical curve, which is sometimes called bell-shaped, because it has a shape rather like that of a section taken through the middle of a bell. The normal distribution is a theoretical distribution; it is never obtained experimentally. It implies, for example, an infinitely large number of observations; and moreover it implies a variable which can take on any value from *minus* infinity to *plus* infinity, though it is true that the values at the extreme ranges occur with a relatively low frequency. In practice we often obtain distributions which resemble the normal closely, but there is no *a priori* reason why distributions of biological measurements should necessarily be of this type. Now one of the assumptions made in performing a *t*-test is that the measurements obtained by the experimenter are a random sample from a normal population. It is obvious that the usefulness of the test is not necessarily destroyed if the parent population fails to be normal, for otherwise the *t*-test would never be valid in practice. The crucial point is how great the departure from normality must be before the test becomes misleading. Unfortunately there is no simple answer to this important problem; but an introductory discussion is given later when some of the shortcomings of the *t*-test are reviewed. In the final resort we may have to turn to a new type of statistical test, in which we do not require any assumptions at all about the form of the frequency distribution of which our data are regarded as a sample.

### Examples of t-Test.

*Example I.*

Wilson *et alii* (1941) wished to find out whether infants whose umbilical cords had been clamped immediately after birth had a lower hæmoglobin value than infants whose

cords had not been clamped until the placenta began to descend into the vagina. It was argued that the latter group of infants would have the advantage of extra placental blood and that this might be reflected in higher hæmoglobin values. The experiment consisted of collecting data on the blood of infants belonging to the two groups described; and the section of this data which shows the hæmoglobin values at the end of the first week of life is given in Table II.

TABLE II.

*Hæmoglobin Values Measured on Two Groups of Infants During the First Week of Life. Group A had the Umbilical Cords Clamped Immediately after Birth and Group B did not have the Cords Clamped until the Placenta began to Descend into the Vagina.*

(Data from Wilson, Windle and Alt, 1941.)[1]

| Group A. | | | Group B. | | |
|---|---|---|---|---|---|
| Hæmoglobin Value in Grammes per Hundred Millilitres. ($X_A$.) | $X_A - 20$. | $(X_A - 20)^2$. | Hæmoglobin Value in Grammes per Hundred Millilitres. ($X_B$.) | $X_B - 22$. | $(X_B - 22)^2$. |
| 18·6 | −1·4 | 1·96 | 22·5 | 0·5 | 0·25 |
| 17·3 | −2·7 | 7·29 | 25·3 | 3·3 | 10·89 |
| 15·7 | −4·3 | 18·49 | 22·0 | 0·0 | 0·00 |
| 22·0 | 2·0 | 4·00 | 22·3 | 0·3 | 0·09 |
| 18·7 | −1·3 | 1·69 | 25·1 | 3·1 | 9·61 |
| 18·1 | −1·9 | 3·61 | 22·8 | 0·8 | 0·64 |
| 18·3 | −1·7 | 2·89 | 23·5 | 1·5 | 2·25 |
| 21·6 | 1·6 | 2·56 | 24·0 | 2·0 | 4·00 |
| 19·7 | −0·3 | 0·09 | 20·8 | −1·2 | 1·44 |
| 21·0 | 1·0 | 1·00 | 31·1 | −0·9 | 0·81 |
| 19·3 | −0·7 | 0·49 | 22·2 | 0·2 | 0·04 |
| 21·0 | 1·0 | 1·00 | 24·7 | 2·7 | 7·29 |
| 18·0 | −2·0 | 4·00 | 20·5 | −1·5 | 2·25 |
| 21·0 | 1·0 | 1·00 | | | |
| 20·9 | 0·9 | 0·81 | | | |
| *Totals* .. | −8·8 | 50·88 | | 10·8 | 39·56 |

Mean, $20 - \frac{8 \cdot 8}{15} = 19 \cdot 41$.
Sum of squares, $50 \cdot 88 - \frac{8 \cdot 8^2}{15} = 45 \cdot 72$.

Mean, $22 - \frac{10 \cdot 8}{13} = 22 \cdot 83$.
Sum of squares, $39 \cdot 56 - \frac{10 \cdot 8^2}{13} = 30 \cdot 59$.

[1] Pooled sum of squares, $45 \cdot 72 + 30 \cdot 59 = 76 \cdot 31$. Pooled degrees of freedom, $14 + 12 = 26$. Pooled variance, $\frac{76 \cdot 31}{26} = 2 \cdot 935$. Variance of mean of Group A, $\frac{2 \cdot 935}{15} = 0 \cdot 1957$. Variance of mean of Group B, $\frac{2 \cdot 935}{13} = 0 \cdot 2258$. Variance of difference between mean of A and mean of B, $0 \cdot 1957 + 0 \cdot 2258 = 0 \cdot 4215$. Standard error of difference between mean of A and mean of B, $\sqrt{0 \cdot 4215} = 0 \cdot 65$. Difference between mean of Group A and mean of Group B, $22 \cdot 83 - 19 \cdot 41 = 3 \cdot 42$. $t$, $\frac{3 \cdot 42}{0 \cdot 65} = 5 \cdot 2$. A $t$ of 5·2 with 26 degrees of freedom has a $P$ of $< 0 \cdot 001$ (Fisher and Yates, 1943, Table 3).

The mean of group B is 22·83 and that of group A, 19·41, so that the former is 3·42 grammes higher than the latter. We now wish to find out whether this difference in favour of group B is "significant"—that is, whether one could expect to find it substantiated by a much more extensive investigation, or whether it has arisen merely by chance, as an accident of sampling. To determine this point we set up a so-called "null" hypothesis to the effect that the two groups have been drawn at random from the same population, and we then examine the data to see whether they can reasonably be explained in terms of this hypothesis. A null hypothesis may be defined as any exact hypothesis that one is interested in disproving.

The basis of the test is to find the ratio of the difference 3·42 to its standard error: this is the ratio $t$.

The variance of group A would be given by $\frac{45 \cdot 72}{14}$ and that of group B by $\frac{30 \cdot 59}{12}$. However, in terms of the null hypothesis, we assume that groups A and B have been drawn from the same population and therefore have the same "true" variance. If the experimental results make this assumption untenable by showing a large discrepancy between the two variances, we cannot use the ordinary $t$-test. In the present example, however, the variances are not widely different, and the best estimate of the population variance is obtained by pooling the estimates from the two groups. The pooled sum of squares is 76·31 and the pooled degrees of freedom are 26, so that the pooled variance is 2·935.

Although the two samples are provisionally assumed to be drawn from the same population, the means of the samples have different variances, because they are based on different numbers of cases—15 in group A and 13 in group B. The variances of the two means are respectively 0·1957 and 0·2258, and the sum of these, 0·4215, is, according to a well-known proposition in statistics, the variance of the difference between the two means. By taking the square root of this variance one finds the standard error of the difference between the two means, and it turns out to be 0·65. The ratio $t$ is the difference of the two means, 3·42, divided by its standard error, 0·65; it is therefore 5·2.

The final step is to evaluate the significance of a $t$ of 5·2 as obtained in this experiment. It has to be considered in relation to the number of degrees of freedom. "Student" worked out the frequency distribution of $t$ as a function of the number of degrees of freedom; a slightly modified version of his results was published by Fisher and is the one now commonly used. On consulting a copy of Fisher's table of $t$ as given, for example, by Fisher and Yates (1943), one finds that there is a probability of less than 1 in 1000 that a difference at least as great as that found between the means would have occurred if the null hypothesis was true. This probability is so low that we reject the hypothesis on which it was deduced—namely, the hypothesis that there is no difference between the two groups; and, with a degree of confidence which, according to one school of thought, we may think of as being measured numerically by the value of $(1 - P)$, we accept the conclusion that the means differ in value. In physiological terms, we conclude that early clamping of the umbilical cord has the effect of making the hæmoglobin value of the infant's blood lower, on the average, at the end of the first week of life than it would otherwise be.

### *Example II.*

E. B. Wright (1946) measured the survival time of nerves which had been removed from various species of animals and deprived of oxygen immediately after removal. Included in his results are those for the survival time of the peroneal nerve of the rabbit and of the cat, and these results are presented in Table III. The mean survival time for the nerve from the cat was 12·4 minutes longer than that of the nerve from the rabbit. Is this difference significant or has it just occurred by chance? This question can be answered by applying a $t$-test.

Even if one does not use a calculating machine, the quickest way of working out the sum of squares in this case is to begin by squaring the original observations as they stand. The total of these squares is 5588 for group A and 8741 for group B. From these totals one must subtract a correction factor to obtain the sum of squares. The correction factor for group A is $146^2$ divided by 4, and for group B it is $337^2$ divided by 14; so that the sum of squares is 259 for group A and 628·9 for group B. The remainder of the calculation is similar to that of Example I, and the conclusion is that there is only one chance in 100 that a difference at least as great as that found between the two means would have been obtained if the two sets of survival times had been drawn at random from the same population. We therefore assert that the null hypothesis should be rejected and that there is a statistically significant difference between the two mean survival times; that is, the nerve from the cat, under the conditions of the experiment, survives longer, on the average, than that from the rabbit.

### *Example III.*

Dripps and Comroe (1947) have investigated the effect on the pulse rate of changing from the inhalation of room

air to the inhalation of 100% oxygen. They worked with normal human subjects. Part of their data is concerned with the effects which occur within the first two minutes of the change. These data are analysed in Table IV.

The type of *t*-test required here is somewhat different from that used in the two previous examples and is identical with the type used in "Student's" original illustration. The observations consist of a series of pairs, the two members of which have been obtained from the same subject. Each subject, therefore, acts as his own control; and if the initial pulse reading is high because of, say, latent hyperthyreoidism, then the second reading will be influenced by the same factor, and one therefore hopes that the difference between the two readings may be free of any influence from this factor. If this is so, the difference in pulse rate is a measure of the effect of changing from the inhalation of room air to the inhalation of 100% oxygen, and is independent of differences between subjects. In the experiment the pulse decreased by 2·67 beats per minute, on the average, when the subjects inhaled 100% oxygen for the given time. The appropriate null hypothesis is that there is no difference between the two rates, and we proceed to inquire whether, if this is so, a difference of 2·67 could reasonably be expected to occur in our sample as a result of chance.

In this case we list the 33 differences between the control reading of the pulse rate and the corresponding reading after the oxygen had been given. We then proceed to calculate several statistics from this series of differences. The mean of the series has already been found; it is 2·67. We also need the standard error of this mean, and we obtain it in the following routine manner. First the values are squared and the squares are added to give a figure of 552. To obtain the sum of squares, as previously defined, we must subtract from this a correction factor which is equal to $\frac{88^2}{33}$. The sum of squares is therefore 317·3, and the degrees of freedom are 32. Hence the variance of the series of differences is 9·916. The variance of the mean of the series of differences will be obtained by dividing 9·916 by the number of observations in the series—that is, by 33. Consequently the variance of the mean is 0·300 and the standard error of the mean is 0·55.

TABLE III.

*The Survival Time under Anoxic Conditions of the Peroneal Nerve of the Cat (Group A) and the Rabbit (Group B).*

(Data from E. B. Wright, 1946.)[1]

| Group A. | | Group B. | |
|---|---|---|---|
| Survival Time in Minutes. ($X_A$). | ($X_A$)². | Survival Time in Minutes. ($X_B$). | ($X_B$)². |
| 25 | 625 | 28 | 784 |
| 45 | 2,025 | 15 | 225 |
| 33 | 1,089 | 35 | 1,225 |
| 43 | 1,849 | 28 | 784 |
| | | 35 | 1,225 |
| | | 23 | 529 |
| | | 22 | 484 |
| | | 22 | 484 |
| | | 17 | 289 |
| | | 20 | 400 |
| | | 30 | 900 |
| | | 30 | 900 |
| | | 16 | 256 |
| | | 16 | 256 |
| Totals 146 | 5,588 | 337 | 8,741 |
| Mean 36·5 | | Mean 24·1 | |
| Correction factor for sum of squares, 5,329. Sum of squares, 259. | | Correction factor for sum of squares, 8112·1. Sum of squares, 628·9. | |

[1] Pooled sum of squares, 259 + 628·9 = 887·9. Pooled degrees of freedom, 3 + 13 = 16. Pooled variance, $\frac{887 \cdot 9}{16} = 55 \cdot 49$. Variance of mean of Group A, $\frac{55 \cdot 49}{4} = 13 \cdot 87$. Variance of mean of Group B, $\frac{55 \cdot 49}{14} = 3 \cdot 96$. Variance of difference between mean of A and mean of B, 13·87 + 3·96 = 17·83. Standard error of difference between mean of A and mean of B, $\sqrt{17 \cdot 83} = 4 \cdot 22$. Difference between mean of A and mean of B, 12·4 $t$, $\frac{12 \cdot 4}{4 \cdot 22} = 2 \cdot 9$. $P = 0 \cdot 01$.

TABLE IV.

*Pulse Rates of Subjects when Breathing Room Air and when Breathing 100% Oxygen.*

(Data from Dripps and Comroe, 1947.)[1]

| Subject Number. | Pulse Rate on Breathing Room Air, in Beats per Minute. ($X_A$.) | Pulse Rate on Breathing Oxygen in Beats per Minute. ($X_B$.) | $X_A - X_B$. | $(X_A - X_B)$². |
|---|---|---|---|---|
| 1 | 78 | 76 | 2 | 4 |
| 2 | 68 | 64 | 4 | 16 |
| 3 | 68 | 64 | 4 | 16 |
| 4 | 66 | 64 | 2 | 4 |
| 5 | 76 | 76 | 0 | 0 |
| 6 | 84 | 84 | 0 | 0 |
| 7 | 76 | 72 | 4 | 16 |
| 8 | 60 | 60 | 0 | 0 |
| 9 | 72 | 72 | 0 | 0 |
| 10 | 108 | 96 | 12 | 144 |
| 11 | 84 | 88 | −4 | 16 |
| 12 | 76 | 76 | 0 | 0 |
| 13 | 68 | 64 | 4 | 16 |
| 14 | 54 | 50 | 4 | 16 |
| 15 | 72 | 70 | 2 | 4 |
| 16 | 74 | 70 | 4 | 16 |
| 17 | 64 | 60 | 4 | 16 |
| 18 | 64 | 64 | 0 | 0 |
| 19 | 60 | 58 | 2 | 4 |
| 20 | 80 | 72 | 8 | 64 |
| 21 | 62 | 64 | −2 | 4 |
| 22 | 72 | 72 | 0 | 0 |
| 23 | 64 | 60 | 4 | 16 |
| 24 | 84 | 78 | 6 | 36 |
| 25 | 76 | 70 | 6 | 36 |
| 26 | 76 | 72 | 4 | 16 |
| 27 | 86 | 84 | 2 | 4 |
| 28 | 60 | 60 | 0 | 0 |
| 29 | 52 | 48 | 4 | 16 |
| 30 | 76 | 76 | 0 | 0 |
| 31 | 78 | 76 | 2 | 4 |
| 32 | 82 | 80 | 2 | 4 |
| 33 | 64 | 56 | 8 | 64 |
| Totals .. .. | 2,384 | 2,296 | 88 | 552 |
| Means .. .. | 72·24 | 69·58 | 2·67 | |

[1] Correction factor for sum of squares, $\frac{88^2}{33} = 234 \cdot 7$. Sum of squares, 552 − 234·7 = 317·3. Variance of differences, $\frac{317 \cdot 3}{32} = 9 \cdot 916$. Variance of mean of differences, $\frac{9 \cdot 916}{33} = 0 \cdot 300$. Standard error of mean of differences, $\sqrt{0 \cdot 300} = 0 \cdot 55$. $t = \frac{2 \cdot 67}{0 \cdot 55} = 4 \cdot 8$. $P < 0 \cdot 001$.

The value of $t$ obtained in this experiment is $\frac{2 \cdot 67}{0 \cdot 55}$ or 4·8, and on consulting the table of $t$ for cases in which there are 32 degrees of freedom, we find that $P$ is less than 1 in 1000. We therefore reject the null hypothesis and conclude that the pulse rate decreases on changing from the inhalation of room air to the inhalation of oxygen.

It is worth inquiring what the result would have been if one had carried through a *t*-test similar to that used in Examples I and II. This would be the appropriate method of analysis if the observations had not been paired. To save space, the detailed figures are omitted, but one may easily verify the fact that the difference between the two means is the same as the mean of the 33 differences, namely 2·67; and that the standard error of the difference of the two means is 2·65, which is considerably greater than the figure of 0·55 obtained above as the standard error of the mean of the differences. The $t$ ratio is 2·67 divided

by 2·65, that is 1·0. This is a $t$ which could well occur by chance, and this analysis therefore leads to the incorrect conclusion that there is no significant difference between the two groups.

It is easy to see, in a general way, why this second analysis is incorrect. The pulse rates of the 33 subjects differed considerably from one another, so that the variance of the mean was relatively high; and this was reflected in a high denominator in the $t$ ratio. But variation between the pulse rates of the 33 subjects is irrelevant to the present problem. The question at issue is simply whether the pulse rate falls as a result of the breathing of 100% oxygen. Subjects numbered 4 and 27 have very different pulse rates, namely 66 and 86 per minute respectively, but they each react to the administration of pure oxygen by a decrease of two beats per minute. In the first method of analysis given above one confines one's attention to the fact that there was this same decrease in the two subjects; but in the second method the outcome is affected by the initial difference between the two subjects—a difference with which the experiment is not concerned.

### The Statistical Treatment of Paired Observations.

The method of pairing used in the above experiment has been successful. If one had merely been given the two sets of 33 pulse rates without having them grouped in pairs, one would not have been able to establish the point that the difference between the two groups was significant. Problems similar to this are commonly found in experimental work, and as a result it has long been a practice to conduct experimental and control observations either on the same subject or else on two subjects, such as litter mates, who are so similar that for the purpose of the experiment they can be regarded as paired. The pairing technique is rightly considered to provide a sound experimental design. However, it may not always be possible to arrange such pairing in an experiment; for instance it could not be done in the experiments discussed in Examples I and II. Further, it is worth pointing out that even if pairing is possible it will not always improve the results. An example can be found in an experiment conducted by Smith and Medlicott (1944). They produced anæmia in rats by feeding them a diet of milk, and they then tested the therapeutic effect of administering iron. The results are given in Table V. If they are examined by finding the standard error of the two means and, from these, the standard error of the difference between the two means, then $t$ is 1·70 and the number of degrees of freedom is 22. But if the paired technique is used, the $t$ value is about the same—1·62, and the number of degrees of freedom is 11. Pairing has therefore not revealed a difference concealed by the first method of examination.

A rule can be drawn up to indicate when the method of pairing will improve the results. If one compares $X_A$ with the corresponding $X_B$ in Table IV, one notes that they are strongly correlated. This can be shown, if necessary, in a formal way, by working out the coefficient of correlation as 0·96. On the other hand, the coefficient of correlation between $X_A$ and $X_B$ in Table V is low; the value in the experiment is even negative (−0·21), but there is no reason to regard this as anything but a chance fluctuation from a true value of zero. Now it can be shown that the difference between the standard error used in a $t$-test on unpaired observations and that used in the corresponding test on paired observations varies with the coefficient of correlation between $X_A$ and $X_B$. If the true coefficient of correlation is 0, there is no difference between the standard errors. If the coefficient is positive—and this is the common situation in experiments in which the paired technique is employed—then the standard error used in the paired technique is the lower of the two. If the coefficient of correlation is negative, then the standard error used in the paired technique is higher. Pairing is therefore successful whenever there is a significant positive correlation between the members of the pairs of observations; but if the coefficient is negative, pairing is of no assistance in establishing a significant difference between the two groups, since it increases the standard error and reduces the number of degrees of freedom used in evaluating $t$. In most cases an experimenter who is familiar with his material can anticipate when pairing will be profitable; but this will not always be possible. As far as the evaluation of the results is concerned, there is no objection to working out the $t$-test by both methods when pairing has been used, and regarding the results as significantly different if either of the two tests classifies them so, and if such a conclusion cannot be ruled out on biological grounds as being absurd.

TABLE V.

*Hæmoglobin Values in Anæmic Rats Before and After Treatment with Iron.*

(Data from Smith and Medlicott, 1944.)

| Rat Number. | Hæmoglobin Value in Grammes per 100 Millilitres of Blood. | |
|---|---|---|
| | Before Treatment. ($X_A$.) | After Treatment. ($X_B$.) |
| 1 | 3·4 | 4·9 |
| 2 | 3·0 | 2·3 |
| 3 | 3·0 | 3·1 |
| 4 | 3·4 | 2·1 |
| 5 | 3·7 | 2·6 |
| 6 | 4·0 | 3·8 |
| 7 | 2·9 | 5·8 |
| 8 | 2·9 | 7·9 |
| 9 | 3·1 | 3·6 |
| 10 | 2·8 | 4·1 |
| 11 | 2·8 | 3·8 |
| 12 | 2·4 | 3·3 |

It has sometimes happened that an experimenter made paired observations and then analysed them as if they were unpaired. In a recent paper, for example, blood counts obtained on the peripheral blood of dogs were compared with those obtained on blood taken directly from the heart (Azarnoff *et alii*, 1951). The results did not show any significant difference between the two groups, but the $t$-test appropriate to paired observations was not made. It is true that this is probably not a question that can be solved by a simple change of statistical tests; that is revealed by the authors' reference to previous work, including some conflicting observations of their own on the guinea-pig, and by their general discussion of the problems involved; but the calculations previously made on the data of Dripps and Comroe show that it is never safe to trust entirely to the test designed for unpaired observations when in fact the observations are paired. There are other cases in the literature in which failure to carry out "Student's" version of the test can be criticized more severely than in the above-mentioned work on blood counts. It is often easier to arrange an experiment without pairing than it is to introduce pairing, and if one goes to the trouble of designing the latter type, one should surely carry out an analysis which will bring to light any advantage that the pairing may have produced.

### Assumptions Made in Applying the t-Test.

The $t$-test has been presented so far as a more or less mechanical operation in the handling of figures. Even in an introductory account of its use, however, mention should be made of four assumptions on which the test is based, for it sometimes happens that one or other of these assumptions cannot be legitimately made in a particular case.

1. The first assumption is that the population from which the samples were drawn has a normal distribution; in other words, the null hypothesis which one accepts or rejects is the hypothesis that the two samples were drawn not merely from the same population, but from the same normal population. Occasionally we know that this assumption of normality is approximately correct; for example, the height of adults is a measurement which we know from many investigations to be distributed in an approximately normal manner. Usually, however, we are not certain that such an assumption applies to the data on which we wish to use the $t$-test; and, indeed, the sample

itself may provide evidence against the assumption. A question arises as to whether the *t*-test becomes invalid when the population from which the samples were taken is not normally distributed.

It is agreed that there may be considerable departure from normality, especially in the direction of skewness of the distribution, without much effect on the general reliability of the *t*-test. Any mathematician who is on his mettle may find exceptions to this statement; but it has not been found to be seriously misleading in practice. Indeed the *t*-test is often applied without any thought at all as to whether the parent populations are normal. This is probably not a dangerous practice unless the experimenter places undue stress on the statistical tests and is in the habit of rejecting without further question any null hypothesis which, according to his experiment, has a probability of less than 0·05.

It is sometimes possible to alter the unit of measurement so that a series of results which had a skew distribution becomes more or less symmetrical. If such a transformation is possible it should be carried out before a *t*-test is performed. An example is provided by the results of Wright *et alii* (1948), who measured the rate of flow of venous blood in the legs. The distribution of the so-called "foot-groin" times was skew, but the distribution of the logarithm of the "foot-groin" times was well fitted by a normal curve. Hence, in performing *t*-tests on samples of this type of data, one should begin by transforming the measurements to logarithmic units.

2. A second assumption which one makes in performing a *t*-test is that the two samples have variances which do not differ to a greater extent than can be explained by random sampling from the same parent population. A test of this assumption is provided by considering whether the ratio of the variances of the two groups—the so-called *F* ratio—is abnormally high. As an example one may consider the data presented in Table V. The variance of the hæmoglobin values of the rats before treatment is 0·1924 and the variance of the corresponding values after treatment is 2·6572, so that the *F* ratio is $\frac{2{\cdot}6572}{0{\cdot}1924}$ or 13·58. If one consults Table V in "Statistical Tables" by Fisher and Yates (1943), one finds that when two samples of 12 members each are drawn from the same normal population there is only a 1 in 500 chance that the ratio of their variances will be greater than 7·00. (In using this Table V for this particular purpose, the *P* value recorded there must be doubled, because in this case we have formed the *F* ratio by placing the larger variance in the numerator, and the table does not provide for this freedom to use one or the other variance in the numerator according to our arbitrary standard.) Clearly, then, the samples have different variances and the usual *t*-test cannot be applied to determine whether their means are different. The modification required in the conventional test, however, is slight in instances such as this, in which the number of cases in the two groups is the same. It simply consists of consulting the *t* table with $(n - 1)$ instead of $(2n - 2)$ degrees of freedom, where $n$ is the number of cases in each group. The answer is approximate only, but adequate for most purposes.

When the number of cases in the two groups is different, the modification is more complicated. The sums of squares cannot be pooled. Variances of the two means are evaluated separately and then added to give the variance of the difference between the two means. From this variance the standard error of the difference between the two means is found, and the *t* ratio is then evaluated in the usual way. At least we may describe this ratio as a *t* value in the sense that it has been obtained by a method which resembles that used in finding *t*; but it is not distributed like *t*. To find approximately that value of the new ratio which should not be exceeded more than five times in 100, on the average, one first reads off from a table the two values of *t* corresponding to a *P* of 0·05 and to the degrees of freedom appropriate to the samples being tested. One then finds a weighted mean of these two values, the weights being proportional to the variances of the means of the two groups. Full details and a worked example are given in a recent book by Cochran and Cox (1950).

These solutions are only approximate. It is perhaps fortunate that a more exact treatment is not often required, because the issues raised constitute a classical problem in mathematical statistics—the so-called Fisher-Behrens problem—and the subject is still controversial. The physiologist, nevertheless, will encounter many instances in which the experimental group is more variable than the control group. This finding, of itself, is evidence against the null hypothesis, and the difference in the variances may have an important physiological meaning. Often, however, the difference between variances is so natural as to amount to a trivial finding and the experimenter will still wish to know whether the means of the series, as well as the variances, are different; for instance, after a therapeutic trial he may not be satisfied with the information that some patients are better and some worse, so that the variance has increased; he will probably want to find out whether there has been an improvement on the average (and probably, also, whether the improvement is significant in the literary as well as in the statistical sense). For the statistical analysis of these problems he may use the modified *t*-test as described above. He may also turn to a new type of test altogether, such as that introduced by Wilcoxon (1945), and modified by the present author to deal with cases in which the numbers in the two groups are unequal (White, unpublished material).

3. A third assumption is that the sampling is random. In the famous Lanarkshire milk experiment designed to compare the nutritive value of raw and pasteurized milk, 10,000 school children were given supplementary milk for four months, some receiving raw milk and some pasteurized, and the observers noted the effect of the supplement on the height and weight of the children. The experiment was a failure, because randomization was not carried out, and each school used either raw milk exclusively or pasteurized milk exclusively. This introduced a possible bias, in that healthier groups of children may have received, say, pasteurized milk; and no *t*-test could circumvent such a bias.

4. A fourth assumption made, so far, is that the experimenter has no reason to know before the experiment is complete whether the control group will give higher or lower values than the experimental group. He carries out what is known as a two-tailed *t*-test, and considers the possibility that the control group may be either significantly lower or significantly higher than the experimental group. This assumption may be unrealistic, but in such a case the adjustment to be made is simple; he can change to a single-tailed test by halving the *P* value obtained by the method so far described. For instance, he may be prepared to accept the view that leaving the umbilical cord without a ligature until the placenta descends into the vagina cannot possibly decrease the infant's hæmoglobin value, and his interest in the experiment is merely to see whether the procedure increases the hæmoglobin value. In such a case he would be entitled to halve the *P* value previously obtained. The use of single-tailed *t*-tests will produce a larger number of significant differences; therefore, in cases of doubt as to whether the appropriate test is single-tailed or double-tailed, the safer course is to use the latter. Some workers invariably use it, and this practice has the virtue that lack of symmetry in the parent distribution may lead to a very misleading result in a one-tailed test, but at the same time may not seriously prejudice the two-tailed test.

### Further Examples of the t-Test.

Current physiological literature contains numerous examples of the use of the *t*-test. A few of these may be mentioned as further illustrations of the methods discussed.

A. J. Lea (1947) compared the level of serum chloride in 16 pregnant mice with that found in 16 non-pregnant but otherwise comparable mice. The values for the non-pregnant mice were significantly higher (*t* was 6·44, degrees of freedom were 30). C. E. Kossmann (1946), from whom some results have already been quoted, compared the blood

pressure readings before and after elevating the arm to drain venous blood from it. He found that the draining of blood decreased the systolic pressure significantly ($t$ was 4·04, degrees of freedom were 31). D. G. Simonsen *et alii* (1947) found that serum magnesium was not significantly higher in adult males than in adult females ($t$ was 1·7, degrees of freedom were 40).

### The Relationship of the Statistical Test to the Physiological Findings of the Experiment.

The words "the difference is statistically significant" are often written or intoned as if they are a guarantee against successful opposition to the conclusions they support. This is a mistaken view. The cornerstone of any experiment is, of course, the basic data; if these are biased or inadequate they cannot be redeemed by statistical tests of any kind. Since it is the physiologist who is trained to collect physiological data, it is he who must accept responsibility for their quality; or, on the other hand, he is entitled to claim that certain data are unacceptable because of flaws in the technique of the experiment, and that he therefore regards the statistical treatment of these data as a meaningless exercise in manipulating figures.

It is clear from the results presented in Example II that there is a difference in the survival times of the peroneal nerves from the rabbit and the cat; but it is still open to any interested physiologist to inquire about such things as whether the animals were of comparable maturity, whether they had a comparable degree of anæsthesia and whether the technique of handling the nerves was the same in the two cases. Again, in Example III, there is a clear demonstration that the pulse rate decreased when the subject changed from breathing room air to breathing 100% oxygen; but it is still pertinent to inquire whether young adults with an average pulse rate of 72 per minute are really in a basal condition, and whether the decrease observed in the pulse rate can be accounted for by the effect of rest. Most people will agree that difficulties of this kind are greater in the cases mentioned than the difficulty of analysing the results statistically. For instance, in Example III, the formal $t$-test could well be replaced by the simple analysis that, since the pulse rate decreased in 22 cases, remained unchanged in nine, and increased in only two, it seems reasonable to conclude that there is a tendency towards a decrease. Again, in looking at the results in Example I, one notes that the highest figure in group A—namely, 22·0 grammes—is higher than only three of the 13 results in group B. It is reasonable to conclude that the hæmoglobin values in group B are higher on the average than those in group A. Once again one would feel safe in dispensing with the formal $t$-test and conserving one's energies for a scrutiny of the physiology of the basic data.

The judgement of the experimenter is always involved in another aspect of the $t$-test—that is, in the interpretation of what is an acceptable level of probability for rejection of the null hypothesis. It is conventional to say that a significant difference has been established if $P$ is less than 0·05, and that the difference is highly significant whenever $P$ is less than 0·01. These rules are meant to help the experimenter and not to dominate him. They certainly do not free him from the responsibility of evaluating the data in the light of current knowledge. He may be wise to brush aside the results of a $t$-test in order to avoid a conclusion which, on general grounds, appears absurd; for striking differences can appear by chance, even when the probability of their doing so is very small, and, moreover, the assumptions made about the data when one decides to use the $t$-test may be unwarranted.

The error of rejecting the null hypothesis when in fact it is true, is known as a Type I error. For example, if it was true that inhalation of oxygen did not decrease the pulse rate, then we should have committed a Type I error in rejecting this hypothesis. It is obvious that we have a useful, though not absolute, guarantee against falling into this error, because we do not reject the hypothesis wantonly, but ask for experimental evidence which fails to line up with it. What of the guarantee against the so-called Type II error, which is the error of accepting the null hypothesis when it is false? It is well to remember that protection against this type of error is often rather limited. This is a warning against arguing that failure to find a significant difference between two groups implies that there is no difference between them. There is an obvious danger of committing a Type II error here. Since $t$ is a ratio, it may be reduced below the level of significance by a relatively large denominator; and a large denominator, indicating a large standard error in the means of the groups, can be produced by carelessness or insensitive technique or by large biological variation over which even the best experimenter may have little control. Therefore a real difference between the groups may pass undetected, and the null hypothesis, though false, may not be overthrown. The utmost caution should be used in pointing to a low $t$ value as evidence that two groups are identical; it is merely evidence that no difference has been established. A recent method for measuring blood volume depends on the assumption that the concentration of erythrocytes is the same throughout the circulation (Mukherjee and Rowlands, 1951). The authors believe that the assumption is valid, and cite in support of this the work by Azarnoff *et alii*, which has already been mentioned. They may well be correct; but, encouraged by the fact that there are some contrary findings in the literature, a critic could reasonably argue that a failure to find differences in the erythrocyte counts of central and peripheral blood is not necessarily good evidence that the counts are the same.

The protection which a statistical test affords against a Type II error is measured by the "power" of the test. The $t$-test is the most powerful test available for the situation for which it was designed—that is, the situation in which we are sampling from two normal distributions of equal variance. We may set up the hypothesis that there is no difference between the means of the two groups. This may be false, and we may therefore be in danger of accepting a false hypothesis; but whatever the true difference between the means is, we are less likely to accept the false null hypothesis when we use the $t$-test than we are when using any other test. In this sense the $t$-test may be referred to as "the uniformly most powerful test". The essential implication here is that the $t$-test enables us to extract the maximum amount of information from the data. No test would rival the $t$-test if it was not for the fact that we sometimes know or suspect or fear that the assumptions necessary for the $t$-test are not reasonable in a particular problem.

### Fiducial Limits.

The purpose of experimenting is to test hypotheses or to measure effects. The $t$-test has been treated so far as a tool for testing hypotheses; but it can also be used in the measurement of effects. The simplest measure of an effect is given by the mean difference between the experimental and control groups. For instance, we may estimate from the results of Example I that tying off the cord before the placenta descended into the vagina had the effect of lowering the hæmoglobin value of the infant's blood by 3·42 grammes per hundred cubic centimetres, on the average. This estimate is a "point" estimate. We can use the $t$ distribution to obtain an "interval" estimate of this same quantity—namely, the difference between the experimental and the control groups. Our calculation involves the four quantities 3·42 (which is the average difference between the two groups), 0·65 (which is the standard error of this difference), 26 (which is the number of degrees of freedom for this standard error), and a quantiy $P$, which we select ourselves, and which is the probability level at which we wish to work in making our estimate. Suppose we select $P$ at the conventional value of 0·05. We consult the $t$ table and find that when $P$ is 0·05 and the number of degrees of freedom is 26, the corresponding $t$ value is 2·056. This $t$ value is then multiplied by the standard error, 0·65, to give a result of 1·34. The interval required stretches from (3·42 − 1·34) to (3·42 + 1·34)—that is, from 2·1 to 4·8. Sometimes the interpretation put on this interval is that there is a probability of only 0·05 that the true difference lies outside this range. This interpreta-

tion is not correct: the true difference either does or does not lie in the range, and is not a fluctuating value about which we can make the above type of probability statement. The true interpretation of a fiducial interval is that if we performed the experiment one hundred times and set up an interval in the same way on each occasion, then we would expect the true difference to lie within the fiducial interval in 95 of the cases. If we had decided to take a smaller risk and set a $P$ value of 0·01, the interval could be calculated in a similar way. It would, of course, be larger; it would stretch from 1·6 to 5·2. It would not overlap zero, because, as we have already found, the difference between the means is significantly different from zero.

There are some branches of statistics—for example, agricultural statistics—in which the making of estimates is usually more important than the testing of hypotheses. I doubt whether this is so in physiology. Perhaps there are only a few people who are interested in the hypothesis that the survival time of the peroneal nerve under the conditions described previously is the same in the cat as in the rabbit. There must surely be fewer still who would want to set fiducial limits to any difference that the experimenter found.

### References.


Azarnoff, D. L., Batty, T. V., Roofe, P. G., and Maffet, M. (1951), "A Comparison of the Number of Circulating Blood Cells in Different Parts of the Circulatory System", *Science*, Volume CXIII, page 363.

Cochran, W. G., and Cox, G. M. (1950), "Experimental Designs", page 91. Chapman and Hall, London.

Dripps, R. D., and Comroe, J. H. (1947), "The Effect of the Inhalation of High and Low Oxygen Concentrations on Respiration, Pulse Rate, Ballistocardiogram and Arterial Oxygen Saturation (Oximeter) of Normal Individuals", *The American Journal of Physiology*, Volume CXLIX, page 277.

Fisher, R. A., and Yates, F. (1943), "Statistical Tables for Biological, Agricultural, and Medical Research", Second Edition. Oliver and Boyd, Limited, London.

Kossmann, C. E. (1946), "The Relative Importance of Certain Variables in the Clinical Determination of Blood Pressure", *The American Journal of Medicine*, Volume I, page 464.

Lea, A. J. (1947), "Serum Chlorides in Pregnant Mice", *Nature*, Volume CLIX, page 469.

Mukherjee, S. R., and Rowlands, S. (1951), "A Direct Method of Measuring the Circulating Blood Volume", *The Lancet*, Volume CCLXI, page 98.

Simonsen, D. G., Westover, L. M., and Wertman, M. (1947), "The Determination of Serum Magnesium by the Molybdivanadate Method for Phosphate", *The Journal of Biological Chemistry*, Volume CLXIX, page 39.

Smith, S. E., and Medlicott, M. (1944), "The Blood Picture of Iron and Copper Deficiency Anemias in the Rat", *The American Journal of Physiology*, Volume CXLI, page 354.

"Student" (1908), "The Probable Error of a Mean", *Biometrika*, Volume VI, page 1.

White, C. (unpublished).

Wilcoxon, F. (1945), "Individual Comparisons by Ranking Methods", *Biometrics Bulletin*, Volume I, page 80.

Wilson, E. E., Windle, W. F., and Alt, H. L. (1941), "Deprivation of Placental Blood as a Cause of Iron Deficiency in Infants", *American Journal of Diseases of Children*, Volume LXII, page 320.

Wright, E. B. (1946), "A Comparative Study of the Effects of Oxygen Lack on Peripheral Nerve", *The American Journal of Physiology*, Volume CXLVII, page 78.

Wright, H. P., Osborn, S. B., and Edmonds, D. C. (1948), "Rate of Flow of Venous Blood in Legs", *The Lancet*, Volume II, page 767.


## APPENDICITIS IN CHILDHOOD.


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APPENDICITIS is a common disease in childhood, as it is in adult life; it is responsible for approximately one admission in every 20 to the Royal Alexandra Hospital for Children. Since the clinical picture in childhood and the appropriate treatment in a particular case differ in some respects from the same problems in adult life, it has been thought worth while to analyse certain records at the above-mentioned hospital. Overall figures regarding admissions, classification and mortality rates cover the four-year period from July, 1946, to June, 1950, inclusive. A more detailed analysis of cases at the hospital during the twelve-month period from July, 1948, to June, 1949, has also been carried out, in order that this paper shall have more authority on such subjects as symptomatology, classification, pathology, age groups *et cetera*.

It is proposed to make but brief and incidental reference to patients with recurrent mild attacks of abdominal pain, as this subject has been covered in a previous article (Stuckey, 1950*a*). In addition, it is desired to point out that the section dealing with treatment has to a large extent already been published (Stuckey, 1950*b*). I am indebted to the Post-Graduate Committee in Medicine in the University of Sydney for permission to include such material in this article.

### ÆTIOLOGY AND PATHOLOGY.

We are still ignorant about the cause of acute appendicitis; some of the factors which have been blamed for initiating the attack are as follows: meat-eating, purified flour, lack of roughage, foreign bodies, laxatives, specific bacteria and preexisting bands or kinks. Very interesting experimental work by A. Q. Wells (1937) seems to have been largely overlooked. He described experiments on rabbits, which have an appendix very similar to that of humans. He found the following: (i) that obstruction of the lumen alone produced a non-inflammatory mucocele; (ii) that deprivation of blood supply alone produced non-inflammatory atrophy; (iii) that injection of bacteria from appendiceal pus, either into the lumen or intravenously, produced no inflammation of the appendix; (iv) that obstruction of the lumen combined with deliberate trauma to the mucosa, the normal bacterial flora thus being allowed to enter the tissues, produced typical obstructive appendicitis with perforation in almost all cases.

I believe there are two primary types of acute appendicitis which can be distinguished from each other in the early stages, the acute obstructive type and the primary inflammatory type.

The acute obstructive type is probably caused as suggested above, and in such cases preexistent narrowing of the lumen or the presence of fæcoliths is undoubtedly important. Inflammatory œdema makes the obstruction complete, tension in the walls of the obstructed, inflamed part finally deprives the whole or part of the muscular wall of its blood supply, and gangrene and finally perforation with peritonitis occur. If the process is moderately slow, if the patient and his bowels are rested, and if the appendix lies in such a position that it can be readily walled off from the rest of the abdomen, a localized abscess occurs; if not, spreading peritonitis occurs, leading if untreated to widespread general peritonitis. In the other type, the primary inflammatory type, possible predisposing factors are lymphoid hyperplasia (common in childhood), trauma to the mucosa by fæcoliths, worms, roughage *et cetera*, and perhaps blood-borne organisms. The result is non-obstructive inflammation of the mucosa, either focal or diffuse, which may spread to the muscle coats, and in rare instances I have seen peritonitis in such cases, without perforation. In the milder grades there is a variable amount of free fluid, which may contain neutrophile leucocytes and organisms, or may be sterile. In these milder cases the condition will subside unless the lumen becomes secondarily obstructed, but further attacks are likely.

Examination of the appendix after an acute attack has subsided often shows remarkably little abnormality. Indeed, in many cases complete resolution may occur, and a microscopic report of "normal appendix" after an interval operation need not make one doubt the original diagnosis. However, true obstructive appendicitis usually ends in death or operative removal, but in the cases in which it subsides one would expect evidence of past inflammation in the form of fibrosis, focal or generalized, with an occasional mucocele. Seldom can one expect the pathologist to substantiate a diagnosis of "subacute" or "chronic" appendicitis. These terms are used in a clinical, everyday sense rather than in a true pathological sense.

### CLASSIFICATION.

The clinical picture and the operative findings show considerable variation. Therefore it is essential that cases be classified into several groups. The simplest classification is into three main groups, as follows: (i) acute appendicitis with perforation; (ii) acute appendicitis without perforation; (iii) recurrent, "chronic" and "interval" appendicitis. There are many statistical analyses in the literature on appendicitis, but most of them include cases among adults. Among those which are confined to children there is wide variation in the percentage of cases falling into each group; the variation is due to factors such as the availability and skill of the local medical practitioners, local habits and hygiene, and general level of awareness of the disease and its symptoms amongst the populace.

Two recent analyses from the United States of America are quoted in Table I for comparison with our own figures (both are confined to children).

TABLE I.

| Source. | Acute. | | Recurrent. |
|---|---|---|---|
| | Appendix Perforated. | Appendix Not Perforated. | |
| Jacobson (Brooklyn), 918 cases, 1934 to 1940 .. .. .. | 22·9% | 72·9% | 4·2% |
| Penberthy *et alii* (Detroit), 1,653 cases, 1928 to 1942 .. .. | 34·4% | 44·9% | 20·7% |
| Royal Alexandra Hospital for Children (Sydney), 2,206 cases, 1946 to 1950 .. .. .. | 4·6% | 63·0% | 31·4% |

It will be obvious that these series of figures are not strictly comparable. For instance, both the American series cover a period extending back to the early 1930's, and it is probable that more recent figures from the same institutions would show smaller percentages of patients with peritonitis. It is also necessary to state that our figure for cases of perforation really includes only those of perforation *plus* drainage; an unknown percentage of cases classified as "acute without perforation" were in fact early cases of perforation in which there was so little spread of pus that the surgeon closed the abdomen without drainage. Nevertheless, I think these figures show a very satisfactory awareness of the disease and its dangers in childhood on the part of parents and local practitioners in this city. Penberthy's series, for instance, includes 292 patients with localized abscess, 183 with early general peritonitis, and 94 with late general peritonitis (of whom 35 were considered too ill for any operation to be performed). We have had no cases of the last-mentioned type in the period from 1946 to 1950.

In my opinion classification must be taken a step further than this if one wishes to discuss comparable groups of cases. It is essential that such classification be made on clinical rather than on histological evidence, because a truly pathological classification is possible only if all appendices removed are examined histologically, which is usually impracticable. I would suggest the following more detailed classification of cases as being desirable, but would point out that it is not at present in use at the Royal Alexandra Hospital for Children. The figures quoted are those for cases in the public wards of the hospital during the period from July, 1948, to June, 1949, each set of case notes having been examined by me in order to make the necessary classification (Table II).

### INCIDENCE AND ASSOCIATED FACTORS.

It is generally stated that males predominate in any large series. This observation is not borne out in our own series, which shows approximately equal numbers of either sex.

#### Age.

It is usually stated that in childhood there is a gradual but steady increase in incidence with each year of age. Jacobson (1942), for instance, found that less than 25% of patients in his series were aged less than seven years. All are agreed that the disease is a rarity under the age of twelve months and uncommon in the second year. In Australia, Howard Williams, of Melbourne (1947), analysed a series of 42 cases in infants under the age of three years. He pointed out the comparative rarity of the disease in this age group, and the additional risks such infants run because of difficulty of diagnosis.

On dissecting our own figures (1948 to 1949) I was surprised to find that the numbers in each age group increased rapidly up to the age of four years when the diagnosis was "acute" appendicitis, but that after that age the numbers remained approximately the same and even fell in later years of childhood. A similar tendency was shown in "subacute" and recurrent cases, but here the peak incidence was not reached until the age of six years. It is admitted that there is probably a tendency for a greater number of older children to be admitted to other hospitals, while the younger ones are more likely to be sent to the Royal Alexandra Hospital for Children. Actual figures are shown in Table III. It should be noted that in this table the diagnosis on admission to hospital does not exactly correspond with the final diagnosis as worked out for the previous table on classification.

TABLE II.

| Classification. | Number of Operations. |
|---|---|
| Acute appendicitis with perforation (27 patients subjected to operation): | |
| (*a*) Established general peritonitis .. .. .. | 0 |
| (*b*) Early spreading peritonitis .. .. .. .. | 13 |
| (*c*) Localized abscess .. .. .. .. .. | 14 |
| Acute appendicitis without perforation (162 patients subjected to operation)[1]: | |
| (*a*) Severe, but appendix unruptured .. .. .. | 35 |
| (*b*) Acute, moderate to mild .. .. .. .. | 90 |
| (*c*) "Subacute" or "chronic"; patient admitted to hospital during an attack .. .. .. .. | 37 |
| Recurrent appendicitis or interval appendicectomy (214 patients subjected to operation): | |
| (*a*) Secondary appendicectomy after previous abscess.. | 8 |
| (*b*) Interval appendicectomy .. .. .. .. | 206 |
| Total .. .. .. .. .. .. | 403 |

[1] There were 36 patients with mild acute appendicitis without perforation who were discharged from hospital without operation.

It is of interest to analyse the average age in the cases of appendicitis with perforation. Howard Williams (1947), in subjects aged under three years, had 36 perforations in 42 cases, and rightly stresses the rapid progress of the pathological lesion at this tender age, the absence of effective omentum, and the difficulties of early diagnosis. In our series (1948-1949) there were 27 cases of appendicitis with perforation, and of these nine patients (one in three) were under the age of four years, although the total number of patients aged under four years represented only 15·6% of patients with acute appendicitis. Even if we include those aged four years we find that in approximately one case in each three admissions to hospital for acute appendicitis, perforation had occurred when the child was submitted to operation. Therefore our figures also bear out the contention that acute appendicitis is a much more dangerous disease in early childhood than it is at a later age.

#### Seasonal Incidence.

Some interesting facts emerge when we study the seasonal incidence of admissions to hospital for appendicitis. The rate rose sharply in February and continued high to the end of May, thereafter showing a gradual fall throughout winter, spring and early summer. This would suggest a maximal incidence in late summer and autumn; but whether this feature is constant from year to year I am unable to state at present. Overseas reports suggest a summer maximal incidence.

## SYMPTOMS AND SIGNS.

Figures quoted in this section refer to the period 1948 to 1949 only.

The only constant symptom is abdominal pain, but even this is so variable in degree that it may be overshadowed by other symptoms in a particular case. The only constant sign is tenderness, but this also is extremely variable, and if the patient is a non-cooperative small child it may be impossible to be certain whether any tenderness is present.

Nevertheless there is a "typical" story which may be elicited in a majority of cases. It was Murphy who first pointed out this "typical" order of appearance of pain, followed by nausea or vomiting, followed by fever, and accompanied by tenderness. The history in many of our cases is not so complete as it should be. Nevertheless in

TABLE III.

*Diagnosis on Admission to Hospital.*

| Age. (Years.) | Number of Subjects. | | Total. |
|---|---|---|---|
| | Acute Appendicitis. | Recurrent Appendicitis. | |
| 1+ .. | 3 | 0 | 3 |
| 2+ .. | 11 | 2 | 13 |
| 3+ .. | 13 | 13 | 26 |
| 4+ .. | 24 | 20 | 44 |
| 5+ .. | 20 | 25 | 45 |
| 6+ .. | 17 | 36 | 53 |
| 7+ .. | 16 | 26 | 42 |
| 8+ .. | 18 | 27 | 45 |
| 9+ .. | 14 | 27 | 41 |
| 10+ .. | 15 | 24 | 39 |
| 11+ .. | 14 | 19 | 33 |
| 12+ .. | 8 | 11 | 19 |
| Totals | 173 | 230 | 403 |

66 (approximately 50%) of 128 cases of acute appendicitis with an adequate history this typical story was present, with virtually no additional symptoms. An additional 16 patients gave the same history with constipation in addition, and 12 patients complained of diarrhœa. In nine cases pain was the only symptom. It should be noted that neither diarrhœa nor constipation can be included in the typical story—it is more usual to have normal bowel actions. In 25 cases nausea or vomiting is said to have preceded the onset of pain. Among this group there were four patients with constipation and five with diarrhœa. For all practical purposes, therefore, one must assume that in childhood pain *plus* tenderness equals appendicitis unless there are very good grounds for deciding otherwise.

There are ten cases in the acute series which have not yet been considered. I wish to stress these cases particularly, because the history began with undoubted acute enteritis which lasted for four to five days, or subsided, prior to the onset of pain, with recurrence of vomiting or diarrhœa, or both together. Five of these 10 patients had a localized abscess at operation, and I feel certain that acute enteritis in which the appendix becomes inflamed as part of the general inflammation is a not uncommon precipitating cause of acute obstructive appendicitis. Such cases are particularly likely to be wrongly diagnosed and to go on to peritonitis.

### Other Symptoms.

There are a number of other symptoms which are not uncommonly mentioned.

#### *Fever.*

In appendicitis fever is usually a sign rather than a symptom, but not uncommonly it is severe enough to be a prominent symptom. When the temperature is high it is often found that the patient has an inflamed throat as well as abdominal symptoms and signs. There is undoubtedly a relationship between the lymphoid tissues of ileum and appendix on one hand and tonsil and adenoid infection on the other. Some authors believe that such cases should be diagnosed as acute mesenteric adenitis and that no operation should be performed; but I am sure that some deaths would occur if this teaching was rigidly carried out. Fortunately in such cases it is usually a non-obstructive type of acute appendicitis which occurs, and it is likely to subside with conservative treatment.

#### *Headache, Lassitude and Malaise.*

Headache, lassitude and general malaise are mentioned in a few cases. Such cases are usually the ones in which high fever and perhaps pharyngitis are present, and which have already been considered.

#### *Urinary Symptoms.*

Urinary symptoms, such as frequency of micturition and dysuria, are occasionally part of the history (eight cases only in this series). It must be realized that an inflamed appendix in contact with bladder or ureter may produce such symptoms, and that a few pus cells and red cells in the urine may also accompany acute appendicitis. In true pyelitis there is usually much more definite evidence on examination of the urine.

#### *Cathartics.*

The use of cathartics is hardly a symptom but it is often part of the story. Our histories are not complete enough for me to quote figures, but it is generally agreed that perforation is more likely to occur in patients who are given cathartics after the onset of pain.

### Pain and Tenderness.

Pain and tenderness are the only outstanding evidence of acute appendicitis, and some further remarks are necessary concerning them. Pain is usually of a generalized nature and is referred to the centre of the abdomen; it is indicated by the hand rather than by a finger, and although it may move to the right iliac fossa in the later stages of an acute attack and in recurrent cases, it often fails to do so. Pain in the right iliac fossa means that the parietal peritoneum in that region is irritated and inflamed, and obviously this can occur only if the appendix lies in that site. Pain may on occasions be present in the right flank when the appendix runs up towards the kidney.

Tenderness is a somewhat unreliable finding for the same reason. One can expect to find pronounced tenderness only when the appendix is easily disturbed by the examining fingers, and this can be expected, with moderate palpation, only when the appendix is anterior to the mesentery of the small bowel and lying free. Deep tenderness may be present, but is often disarmingly slight, when the appendix is behind the caecum or the mesentery or in the pelvis.

When tenderness is uncertain, one should always palpate carefully the right flank, and deep pressure must also be applied above the pubis on both sides. It is always wise to make a rectal examination, and it becomes essential if tenderness elsewhere is vague or uncertain. Rectal examination in itself is a disturbing and somewhat painful procedure to a small child, but with patience it is usually possible to obtain evidence of tenderness, or of a mass, if the appendix is in the pelvis, or even higher in the abdomen in small children. Bimanual palpation is sometimes possible.

In cases in which there is no definite tenderness in the iliac fossa I have found that there is often an area of referred tenderness in the region of the middle third of the right rectus muscle (and sometimes also the left), slightly below rather than above the umbilicus. It requires moderately firm palpation to elicit and is easy to overlook. It is held by some (Aird, 1945) that this is a sign of mesenteric lymphadenitis rather than of appendicitis; but I have found it associated with acute appendicitis too often to agree that it can be used as an argument against operation. In eliciting tenderness in a small child one should not rely on verbal answers so much as on signs of discomfort produced by one's fingers.

Muscle guarding must also be regarded as an inconstant sign. It will occur only if the parietal peritoneum in that area is inflamed, and one cannot expect muscle guarding when the appendix is not accessible to the anterior abdominal wall. Over an area of localized peritonitis there is usually localized guarding, and in general peritonitis in its early stages there is usually generalized guarding. Sometimes generalized tenderness and guarding are found in the presence of free fluid which is not yet purulent.

Rebound tenderness I regard as important in a cooperative patient: but to elicit it requires at least a passive child, and preliminary quiet, deep palpation prior to the sudden removal of the fingers. When it is present there is some serious inflammatory lesion present within the abdomen. I am not impressed with other special signs, such as cutaneous hyperæsthesia or the psoas, obturator or Rosving sign, in childhood.

### Position of the Appendix.

The relative frequency of the various positions in which an appendix may lie can be established only if all the surgeons at a hospital make a point of noting the position, in all cases, at operation before the appendix has been displaced into the wound. This often requires palpation as well as inspection, and I can give you no complete figures from this hospital. Figures quoted in various articles are so variable that it is obvious that no standard procedure has been followed in describing the position in such series. For instance, McNeill Love (1947) in his booklet quotes (not personal observation) "retrocaecal" 70%, pelvic 27%, others 3%. On the other hand, O'Connor and Bessie (1945) quote in 2000 cases of their own, "medial" or pelvic 73·6%, retrocaecal 23%, retroperitoneal 3·4%.

To standardize such descriptions one must first have a clear understanding of what is meant by the terms used. For instance "retrocaecal" in one of the above-mentioned series must obviously include positions more properly called "subcaecal". To my mind the retrocaecal appendix is the one behind the caecum and therefore of necessity also retroperitoneal. I should like to suggest the following terms in describing and classifying the position in which the appendix is found. (i) Anterior or medial: lying free, except for adhesions, with a complete mesentery, and in front of the mesentery of the intestine, its tip being anterior or medial. (ii) Retromesenteric: lying free, except for adhesions, with a complete mesentery, but behind and below the mesentery of the intestine, its tip being directed to the left. (iii) Pelvic: also lying free, except for adhesions, with a complete mesentery, its tip being in the pelvis. (iv) Subcaecal: lying curled up in the right iliac fossa, with a partial or complete mesentery, partly obscured by the caecum. (v) Retrocaecal: lying hidden behind the caecum, with no mesentery, and completely retroperitoneal except occasionally the tip, which lies near the right kidney. (vi) Paracolic: lying in the right paracolic gutter, in part or in whole, with its blood supply passing behind the caecum to reach it, and at least partly retroperitoneal. In our series the surgeon has seen fit to mention the position in only 79 cases out of 403. Of these, the appendix was pelvic or retromesenteric in 15, subcaecal or partially retrocaecal in 22, and retrocaecal or paracolic in 42. These figures are obviously not complete enough for any deductions to be made. However, in a series of my own, of 100 patients with recurrent abdominal pain, submitted to operation, the frequency of the different positions of the appendix was as follows: anterior in 13 cases, retromesenteric in 20, pelvic in 17, subcaecal in 23, retrocaecal in 26, paracolic in one.

### Diagnosis.

The diagnosis of acute appendicitis is usually possible on purely clinical evidence, and to a large extent has therefore already been considered in the discussion of symptoms and signs. But several additional points must be stressed.

A complete examination of the patient is essential, because a child who presents with abdominal pain and vomiting may be suffering from conditions outside the abdomen, and frequently medical rather than surgical in nature.

The temperature and pulse rate are not much help in early cases. An obstructed appendix may not cause early fever or raised pulse rate. On the other hand, a temperature up to 103° F. may be due to appendicitis, but one should suspect some other disease (for example, pneumonia) when both pulse rate and temperature are much elevated. A white cell count is often a help. In any case of severe appendicitis it is likely to be raised to 15,000 or more per cubic millimetre, with pronounced neutrophile leucocytosis, and the figure may reach 30,000 or more per cubic millimetre when suppuration is present. But it may be within normal limits. One can only advise that when the leucocyte count is either substantially normal or extremely high one should carefully reassess the diagnosis, without automatically excluding appendicitis.

The urine should be examined to exclude frank pyelitis, but a few red cells or leucocytes should not cause one to abandon the diagnosis of appendicitis. It is also wise to remember that a child may suffer from recurrent pyelitis in addition to appendicitis.

There is one other sign which should never be overlooked, and that is the state of the tongue and the breath. It is not sufficient to look at the tongue; one should also smell the breath. In the absence of signs of tonsillitis, foul-smelling breath and furred tongue would make me decide to operate in a case in which other signs were indefinite. On the other hand, it is possible to have serious inflammation of the appendix with a clean tongue and breath, so operation should not be postponed merely because this sign is absent.

Howard Williams (1947) points out that the child with appendicitis tends to lie quietly on its side or back and resents disturbance, but the child with tonsillitis, gastro-enteritis *et cetera* is restless and constantly moving about.

That diagnosis in childhood is not easy is shown by the delay in admission to hospital. Excluding the cases which occurred after generalized acute enteritis and in which a history of illness of up to fourteen days' duration was obtained on admission to hospital, I find on dissecting our figures for 1948-1949 that the overall delay from first symptom to admission to hospital was approximately forty-eight hours for the whole series. This figure is too high for safety; at forty-eight hours the appendix which is going to perforate will usually have already done so. This is proved by the fact that our patients with early spreading peritonitis had an average history of only forty-one hours' duration on admission to hospital, and some perforations had occurred at twenty-four hours. Patients with a localized abscess had a history of sixty-three hours' average duration on admission to hospital, and the condition should have been recognized earlier. Duration of symptoms will be referred to again in the discussion of mortality.

To sum up, I should like to stress that in childhood abdominal pain with anorexia, nausea or vomiting should be considered as due to appendicitis until proved otherwise. I am also in entire agreement with Gardner and Sapp (1942) when they assert that so variable is the clinical picture that there is no greater fallacy than that of attempting to forecast the acuteness of the lesion by the acuteness of the signs and symptoms.

### Differential Diagnosis.

In the child many of the acute surgical conditions which may occur in the adult can be largely overlooked. I refer to such diseases as salpingitis, ectopic pregnancy, endometriosis, twisted ovarian cyst, ruptured peptic ulcer, cholecystitis, pancreatitis, volvulus of the sigmoid, and diverticulitis of the colon. Admittedly some of these may on rare occasions occur in childhood, as clinical curiosities. On the other hand, many conditions outside the abdomen proper may confuse the issue in childhood, and it is proposed to deal only with some relatively common problems in diagnosis.

#### *Medical Conditions which Must Be Excluded.*

1. In acute tonsillitis, nasopharyngitis and the early stages of acute specific fevers, the patient may have abdominal pain and vomiting, with no complaint about the sore throat. General signs of toxæmia are usually greater

than in early cases of appendicitis, pain is predominantly epigastric as a rule, and there is no real tenderness in the abdomen.

2. Influenza may start abruptly with abdominal pain and vomiting, which may be oft-repeated. There may be not much cough or coryza. The presence of an epidemic of "gastric" influenza puts one on guard. Again the pain is usually epigastric and is relieved by vomiting. Pain and tenderness are vague and generalized, and not restricted to the abdomen. There is no leucocytosis.

3. In food poisoning and in dietetic indiscretions the pain is colicky, but vomiting is usually the most prominent symptom. There is usually no fever and no real tenderness. The history may reveal others simultaneously affected, or evidence of over-eating some particular food.

4. In the early stages of acute entero-colitis or dysentery there may be no diarrhœa. Sudden fever, pain and vomiting may suggest appendicitis. Tenderness if present is likely to be most pronounced over the descending colon. A few hours' delay may reveal the characteristic motions, and organisms may be grown from the stools.

5. Typhoid and paratyphoid fevers are usually slower in onset, but the surgeon may be asked to examine an obviously "toxic" child with some abdominal distension and tenderness for whom no diagnosis has been made. There is something about these cases which puts one on guard. The patient looks too ill for the symptoms described. The tenderness is rather vague. There is time for a leucocyte count, and suitable tests will reveal the correct diagnosis.

6. The patient with early rheumatic fever often complains of abdominal pain, and tenderness may be present, but this is usually rather generalized. Pain may be in the hip joint or spine rather than true abdominal pain. The picture of appendicitis is rather indefinite, and the general toxæmia more than one would expect. There is usually time for a leucocyte count and erythrocyte sedimentation test.

7. In pneumonia, or basal pleurisy, or pleurodynia in the right lung pain is referred to the abdomen, sometimes mainly to the right iliac fossa. The patient is obviously "toxic" and the high pulse rate and temperature, combined with the type of respiration, help to put one on guard. The pain is unilateral from the start, and this should be viewed with suspicion. Lung signs may be minimal. An X-ray examination may help.

8. Pyelitis may be ushered in with fever, vomiting and pain in the side. The point of tenderness is rather high and includes the renal angle. Pain is unilateral from the start. Urine examination usually reveals the diagnosis. Rigors are not uncommon.

9. In infective hepatitis jaundice takes some days to develop. There may be much vomiting and epigastric pain. The liver may be tender and is often obviously enlarged. The iliac fossa should not be tender. Nevertheless I am sure most of us have removed an appendix in such cases.

10. In the diagnosis of cyclic vomiting, recurrent acidosis or "migraine", the characteristic recurrent nature of the story and the absence of real tenderness may help. Examination of the urine shows acidosis out of proportion to the vomiting. Headache is usually present also. Most children with this malady do in fact end up with an appendicectomy "just in case".

### *Surgical Conditions To Be Excluded.*

Most of the surgical conditions are considerably less common than appendicitis, and in some it perhaps does not matter much so long as the abdomen is opened and the disease is recognized. However, a second incision may be needed, and one should try to exclude these diseases if possible.

1. Obstructed hernia of course is usually obvious, but inspection and palpation of hernial orifices should not be overlooked. A small Richter's type hernia may be impossible to exclude.

2. Intestinal obstruction can easily be diagnosed as acute appendicitis in its early stages, and as general peritonitis in late stages, especially if the seat of mischief is in the right iliac fossa. It may in fact be due to preceding appendicitis. A plain X-ray film is worth remembering.

3. Primary peritonitis is commoner in small infants, in whom appendicitis is rare. Theoretically such a condition could be treated by antibiotics alone; but he would be a brave surgeon who refrained from operating even if he felt appendicitis could be excluded. Suprapubic drainage is warranted.

4. Regional ileitis occurs in childhood, and in acute cases is usually indistinguishable from appendicitis until the abdomen is opened. The typical segment of the bowel, with its œdema, redness and fibrin deposits, is easily recognized. The condition usually subsides with conservative treatment in childhood.

5. Acute mesenteric lymphadenitis is an undoubted clinical entity, but in my opinion it is not common. It may be indistinguishable from acute appendicitis, and in any case I believe operation advisable; appendicectomy often seems to lead to prompt remission of symptoms. In my opinion this diagnosis should not be made merely because there are a few enlarged glands in the ileo-caecal region (they may be due to the appendix), but only when all the lymph glands in the mesentery are evenly and distinctly enlarged and pink.

6. In deep iliac lymphadenitis, usually with abscess formation, the patient may have an insignificant pustular lesion on the foot, leg, buttock or perineum, and the inguinal glands may escape inflammation. The pain and tenderness and perhaps a mass suggest localized appendiceal abscess. It is important to recognize these cases, as the correct approach for drainage is extraperitoneal.

7. Right renal or ureteric obstruction by stone or aberrant vessel or undue mobility may cause symptoms leading to an unnecessary appendicectomy. The renal colic should be recognized by its unilateral nature and typical distribution, and if it is suspected a thorough investigation of renal function is needed. I am sure, however, that we have all made mistakes in such cases.

8. Epigastric hernia or epiplocele (a tiny protrusion of extraperitoneal fat through a small gap in the *linea alba*) is easily overlooked. However, the pain is accurately localized by the patient, and careful palpation in the midline will reveal the tender little lump. Operation is easy.

9. Osteomyelitis of the pelvis, the sacrum, or the head of the femur may cause confusion. Provided that the surgeon thinks of it, careful palpation will reveal the fact that the main tender area is not abdominal.

10. Rarer surgical conditions need be only briefly mentioned, but are occasionally causes of error, unlikely to be correctly diagnosed: (i) trauma to the abdominal wall or to internal organs; (ii) acute pancreaitis; (iii) Meckel's diverticulitis; (iv) intussusception in older children; (v) perforations due to swallowed foreign body; (vi) anomalies of intestinal rotation, with partial obstruction; (vii) mesenteric cysts or tumours; (viii) ovarian cysts or tumours; (ix) torsion of a testis, especially if ectopic; (x) retroperitoneal hæmatoma, cyst or tumour.

### Mortality Rates.

In the series of 2206 cases from 1946 to 1950 there were seven deaths, a mortality rate of 0·3%. If the "chronic" and recurrent cases are excluded the rate becomes six in 1514 cases, or 0·4%. The seven deaths were distributed as follows: spreading peritonitis, 4 deaths in 49 cases (8·2%); localized abscess, 1 death in 52 cases (1·9%); non-perforated appendix, 2 deaths in 2105 cases (0·1%). The mortality rates in other series of cases of acute appendicitis in childhood are quoted for comparison (Table IV). A summary of the history in our fatal cases brings out points of interest.

Case I.—A.N., aged two years and four months, was admitted to hospital on January 22, 1947, with the diagnosis of gastro-enteritis of three days' duration. Operation on the fourth day disclosed a gangrenous retroileal appendix with pronounced inflammation of the caecum and the terminal portion of the ileum. Appendicectomy with drainage was followed by abdominal distension and paralytic ileus. Death

occurred three days after operation, with terminal hyperpyrexia. Autopsy disclosed paralytic ileus and mucosal ulcers in the inflamed caecum and terminal portion of the ileum.

CASE II.—R.K., aged two years and three months, was admitted to hospital on July 5, 1947, with the diagnosis of acute appendicitis of two days' duration. A similar illness had occurred a week earlier, lasting five days. Board-like rigidity was present, and at operation early general peritonitis was found with a retrocaecal, gangrenous appendix; this was removed and drainage was instituted. Death occurred two days later, with abdominal distension, ileus and terminal hyperpyrexia. No autopsy was granted.

CASE III.—S.R., aged five and a half years, was admitted to hospital on September 16, 1947, for removal of the appendix subsequent to drainage of a localized abscess three months earlier. The child had no symptoms on admission to hospital. Operation disclosed a retrocaecal appendix with numerous adhesions near by. It was removed. The child developed abdominal distension and ileus and died seven days after operation with terminal hyperpyrexia. Autopsy disclosed paralytic ileus and recent general peritonitis.

TABLE IV.

*Mortality Rate in Acute Appendicitis in Childhood.*

| Authors. | Unruptured Appendix. | Local Abscess. | Spreading Peritonitis. |
|---|---|---|---|
| Oberhelman and Austin (1944) | 0% (?) | 2·8% | 7·3% |
| Jacobson (1942) | 0·2% | 0% | 5·2% |
| Penberthy *et alii* (1942) | 0·4% | 3·6% | 9·7% |
| Ladd and Gross (1944) | 0·4% | (6·9%) | |

CASE IV.—C.Q., aged seven years, was admitted to hospital on October 21, 1947, with the diagnosis of recurrent mild appendicitis, for interval operation. The child had no symptoms on admission to hospital, but had recently recovered from severe pneumonia. Operation disclosed a completely retrocaecal appendix, which was removed with difficulty. The patient collapsed under anæsthesia and died before leaving the operating theatre. Operation had lasted sixty minutes. As this was a coroner's case, no autopsy was performed. Death was ascribed to myocardial failure.

CASE V.—B.E., aged three and a half years, was admitted to hospital on November 26, 1947, with the diagnosis of primary peritonitis, probably pneumococcal. This child had had six attacks of "pneumonia" in eighteen months, and on this occasion there was a three-day history with symptoms suggesting pneumonia or septicæmia. On the child's admission to hospital, generalized tenderness and guarding were present, and operation disclosed a ruptured retrocaecal appendix with general peritonitis. The child died three days later with apparent toxæmia due to the peritonitis. There was no abdominal distension. Terminal hyperpyrexia occurred. Autopsy confirmed the diagnosis.

CASE VI.—J.T., aged eighteen months, was admitted to hospital on March 2, 1948, with the diagnosis of "gastro-enteritis" of four days' duration, abdominal distension having been present for two days. Operation one day later disclosed intestinal obstruction due to a ruptured pelvic appendix with a localized abscess in the pelvis. Appendicectomy and drainage failed to relieve the distension. Death occurred three days after operation, with terminal hyperpyrexia. Autopsy disclosed paralytic ileus only, and some generalized œdema from excessive intravenous therapy.

CASE VII.—C.G., aged two years and three months, was admitted to hospital on March 14, 1949, with the diagnosis of probable ruptured appendix; the history was of two days' duration, and the child's abdomen was slightly distended, and tenderness was present in the right iliac fossa. At operation a ruptured pelvic appendix was removed; free pus was present, but the abdomen was not drained. He did well for two days, but on the third day his abdomen had to be reopened for obstruction due to adhesive peritonitis. No abscess was found. The patient did not settle down, and his abdomen remained distended; he had paralytic ileus and fever and died on the twelfth day. The post-mortem findings were several small localized collections of pus, adhesive peritonitis and probable mechanical obstruction in the terminal portion of the ileum.

The long duration of symptoms on the patient's admission to hospital, mainly due to faulty diagnosis, is of significance in mortality rates. Of these seven deaths one occurred at "interval" appendicectomy and is one of those accidental "anæsthetic" deaths which occur from time to time. One patient who died had been submitted for residual appendicectomy after a previous operation for drainage of an abscess, and had no symptoms at the time of admission to hospital. Four of the others had ben ill for several days prior to their admission to hospital, and the fifth had a two-day history.

It will be noted that four of the five deaths in cases of ruptured appendix were those of patients aged under two and a half years, and the other patient was aged three and a half years. This surely substantiates the bad prognosis in early childhood, already mentioned, and attributed mainly to difficulty in diagnosis in such patients. Most of these five cases were provisionally diagnosed as some other disease, and the patients were admitted to medical rather than to surgical beds. Ladd and Gross (1944) quote the mortality rates according to age of the patient as follows: birth to one year, 50%; one to two years, 20·8%; two to four years, 9·1%; four to six years, 3·5%; six to twelve years, 1·2%.

I should also like to point out that the position of the appendix in all the fatal cases was either retrocaecal, retro-ileal or pelvic, and this was also surely a factor in the delayed or wrong diagnosis.

## TREATMENT.

Treatment needs to be considered under the following headings: (i) treatment in uncomplicated cases; (ii) treatment of localized appendiceal abscess; (iii) treatment of patients with spreading peritonitis; (iv) post-operative management; (v) treatment of post-operative complications.

### Treatment in Uncomplicated Cases.

All authorities are agreed on the need for early operation in acute uncomplicated appendicitis in childhood; operation should be carried out, as an urgent measure, as soon as diagnosis has been finalized. When there are mild recurrent attacks, it is agreed that operation, preferably between attacks, is best, and in my opinion this remark holds good for cases in which mesenteric lymphadenitis is suspected.

Operative procedure is more or less standardized throughout the world, but comments on a few debatable points are worth while.

1. The incision. In this hospital the McBurney muscle-splitting incision is almost always used. It gives direct and adequate access to the caecum and the base of the appendix in almost all cases. It can be enlarged, if need arises, either medially by cutting into the rectus sheath and pulling that muscle medially, or laterally by cutting across muscle fibres of the internal oblique and transversalis muscles parallel to the iliac crest. Neither method harms the nerve supply of muscles. If an appendix is known to be retrocaecal or paracolic, the more lateral muscle-cutting incision of Rutherford-Morrison gives better access. If pelvic disease is suspected, one should choose the paramedian incision; but I do not think a small child should be given a paramedian scar unless it is essential. In my opinion Battle's incision has nothing to recommend it.

2. The appendix stump. This is usually crushed, ligated and then buried with a purse-string suture in the caecal wall. This is said to produce a tiny abscess in the wall of the caecum, which ruptures into the lumen. In practice it never causes any worry. The application of carbolic acid and spirit to the lumen is optional. Most of our surgeons have ceased using this procedure in routine cases. If the caecal wall is inflamed, friable and œdematous, it is often unwise to try to bury the stump, and it may lead to troublesome hæmorrhage. One need not hesitate to leave the ligated stump free in such cases; it becomes tucked away under the caecum and causes no trouble, provided one does not order aperients or enemata early in the post-operative period.

3. Retrograde removal. When the appendix is partly or wholly without a mesentery, and is lying behind the caecum or in the paracolic gutter, it is not always possible to pull

the caecum up sufficiently to remove it in the usual way. If one can incise the peritoneum on the outer side of the caecum and appendix in such cases, the caecum can be rolled medially and the appendix can be peeled off its wall and then its blood supply can be ligated in the usual way. But if access is insufficient for this procedure, retrograde removal becomes necessary. The technique is well known and need not be further dealt with here. I should merely like to comment that the retrograde removal of an inflamed appendix can be a difficult and worrying procedure, and the more access one has, the better.

4. Adhesions. The tip and body of the appendix will not always readily come into view, but gentle traction on the base will show where it is located. Recent adhesions are easily and safely broken down by blunt finger dissection. Old adhesions or congenital folds or bands may need to be cut, vascular areas being avoided if possible. In this way the appendix is freed until its mesentery can be ligated. When the swollen tip is wrapped in omentum (which is not common in children) it may be gangrenous or ruptured, and it is best to remove that portion of the omentum with the appendix, by multiple ligation of the omental vessels, in sections.

5. Drainage. Even though the appendix is severely inflamed and free fluid is present in abundance, I would not recommend drainage in unperforated appendicitis. There is an occasional case in which actual peritonitis may be present with a severely inflamed but unruptured appendix; but even in these cases, in my opinion, removal of the appendix is all that is necessary. It is possible for a post-operative localized abscess, usually in the pelvis, to develop even after a moderately inflamed appendix has been removed, but it is not possible to predict the cases in which this complication will develop.

6. No obvious disease. When the appendix is apparently normal, one should make a habit of looking for other abnormality, in particular Meckel's diverticulitis and mesenteric lymphadenitis, and also send the appendix to the pathologist for examination.

### Treatment of Localized Appendiceal Abscess.

Localized appendiceal abscess occurs when the appendix has perforated, but by virtue of either the slowness of the pathological process or the secluded situation of the appendix the patient has succeeded in walling off the resulting abscess from the rest of the peritoneal cavity. I will consider the following types of case: (i) a localized mass is felt in the iliac fossa prior to operation, perhaps only when the patient has been anæsthetized; (ii) a localized mass is recognized in the pelvis prior to operation, by rectal examination; (iii) the abscess is found at operation, in the iliac fossa, in the paracolic gutter, behind the mesentery of the intestine, or in the pelvis.

1. If a mass can be felt through the abdominal wall prior to operation, many authorities advise conservative treatment, especially for adults. But such patients require very careful hospital observation, and many of them still require operation because the abscess is enlarging and threatening to rupture into the general peritoneal cavity. In this hospital such patients are almost invariably operated on urgently. The aim is merely to provide an exit for the pus, which is under tension. The appendix is not usually removed, although it may be in some cases in which removal can be easily performed. The incision should be small and should be directly over the swelling, the deeper muscles are best cut across in line with the cut in the external oblique, and the incision is often virtually extraperitoneal. If one makes a long incision and if one persists in removing a difficult appendix (these appendices are often retrocaecal), one runs a grave risk of breaking down adhesions and producing general peritonitis.

In these cases drainage should always be used. It is my practice to shorten the tube daily after the second or third day, and not to reinsert any tube after the original falls out in five to seven days. There will be sufficient track for pus to escape if it is still being produced. Drainage should be through a separate stab wound in the flank, unless a very small incision has been used. The appendix, if it has not been removed, is left until a second operation three to six months later, when there are usually old adhesions to divide before it can be removed.

2. If a definite pelvic abscess can be felt prior to operation, it raises a problem. If one operates, preferably by paramedian incision, it can be dealt with as described in the next section; but one will be traversing unsoiled areas of peritoneum in order to locate and drain it. If one can be sure of the diagnosis, it is likely that by waiting and by treating the patient on conservative lines the abscess will either resolve or point in the anterior wall of the rectum, in which case it can be safely drained *per rectum* by blunt dissection and tube drainage. I believe myself that these are the only patients who should usually be treated conservatively in childhood. The treatment demands (i) careful observation in hospital and repeated examination of the patient, including rectal examination; (ii) the administration of watery fluid only by mouth, no aperients, and the adoption of Fowler's position; (iii) the intravenous administration of fluid if the patient is "toxic" or dehydrated, and gastric suction if vomiting is present; (iv) the use of chemotherapy and antibiotics according to one's discretion. Occasionally such a patient will give evidence of increasing tension and enlargement of the abscess, and one will be forced to operate before it points in the rectum. As a rule in such late cases the abscess can be drained through a small suprapubic incision without soiling the rest of the peritoneum, because it will have enlarged upwards enough to be beneath the lower abdominal wall. Drainage only should then be attempted. Pelvic abscess secondary to appendicectomy is not uncommon and should be dealt with on the same lines. It is a complication which sometimes occurs in the less severe cases, when least expected.

3. When an appendiceal abscess is discovered after the belly has been opened, the truly conservative surgeon will close the wound and wait. I do not advise this course. In any case, often one is not sure whether there is an abscess or not, until, when some of the adhesions are broken down with the finger, pus wells into the operation area. A sucker is needed and all visible pus is rapidly removed. After that it is wise to continue with appendicectomy, provided one is confident that one is not soiling any areas of peritoneum not already soiled. If appendicectomy appears likely to be difficult, I believe the appendix should be left, and this applies whether the abscess is pelvic, retromesenteric, subcaecal or retrocaecal. I believe drainage is required in all these cases, whether or not the appendix has been removed. The drainage tube should be brought out through a separate stab wound, as near as practicable to the abscess. This usually involves either suprapubic drainage or a drain in the iliac fossa above and lateral to one's incision. The main incision is then closed after 100,000 units of penicillin, with or without sulphonamide powder, have been dusted into the peritoneal cavity, which has been soiled. It is wise to put a small glove drain down to the deeper layers of the wound and to dust them also, as these wounds often suppurate mildly prior to healing. For this reason also it is wise to use interrupted sutures, including those in the skin. The glove drain is removed after three days. The intraperitoneal drainage tube is shortened daily till it falls out, as has already been described.

#### *Conservative Treatment of Appendiceal Abscess.*

I have outlined my own ideas about treatment in cases of appendiceal abscess. It is as well to acknowledge that we are on debatable ground. In adults many authorities advise treating the localized abscess conservatively, hoping that it will subside and be reabsorbed. However, not many favour this course in childhood, and it is seldom attempted in this hospital.

Oberhelman and Austin (1944) advise conservative treatment of the local abscess; even if the abdomen has been opened before a walled-off abscess is found, they advise closure without interfering with the abscess in any way. If after conservative treatment it is obvious that the

lesion is spreading, then they perform drainage only. They reported two deaths among 74 patients so treated.

Jacobson (1942) does not operate on a patient with a localized abscess if symptoms are of three days' duration or longer, unless the abscess is obviously enlarging; but on reading his article one finds that in 15 out of 18 such cases the abscess was in fact considered to be enlarging, and operation was performed. Penberthy *et alii* (1942) advise discretion; if the abscess is large they perform simple drainage, with appendicectomy later. Ladd and Gross (1944) do not advise conservative management for children.

### Spreading Peritonitis.

1. Spreading peritonitis usually means early general peritonitis because the appendix has ruptured before the peritoneum has had time to seal off the area. I do not think there is any question that in childhood these patients require early operation, for two reasons. Firstly, it is impossible to be sure beforehand that peritonitis is in fact present, and if operation succeeds in removing an appendix which was about to rupture, so much the better. Secondly, I believe that one must remove the factory which is still producing pus if one wishes to avoid established or late general peritonitis.

Immediate operation is therefore undertaken, and it is usually found that the appendix, not being in a walled-off abscess, is relatively easily removed. It should almost always be removed in such cases. Occasionally what was originally a localized abscess has just ruptured into the rest of the peritoneal cavity, and in such cases it may be wise to leave the appendix if its removal is likely to be difficult. All visible pus should be sucked out and an attempt made to judge the amount of spread. In the early case, in which only a little pus has been found and the appendix has been removed, I believe one should close the wound without drainage, after introducing penicillin and sulphonamide powder. One learns to respect the ability of the peritoneum to deal with moderate doses of pathogenic organisms, once the factory producing them has been removed. When there is obviously a considerable amount of soiling, the case really becomes one of established general peritonitis and is dealt with as set out below.

Some of these patients will undoubtedly end up with a post-operative secondary abscess, usually in the pelvis, but I feel sure that this does not happen any more often than it would if drainage had been used at the original operation.

Penberthy *et alii* (1942) advise removal of the appendix in these cases, unless it is difficult of access, and they favour drainage in addition. Oberhelman and Austin (1944) also advise in these cases early removal of the appendix with drainage. They propound the interesting theory that if the point of rupture is in the distal two-thirds of the appendix the leak usually stops, and such conditions usually end as a walled-off localized abscess; but they believe that when the whole appendix is obstructed and the rupture is near the caecum, the leak will not stop, and these are the conditions which go on to produce general peritonitis.

2. Established general peritonitis is rare in this hospital, thanks to the awareness of our general practitioners and of the general public. Such patients may in fact be already moribund on their admission to hospital. They have had a ruptured appendix without localization for long enough to have the abdominal distension, the constipation and the vomiting of paralytic ileus. They are obviously "bad risks" and require resuscitation, including adequate intravenous therapy, before as well as after operation. This was the type of case (but not in children) which inspired the Oschner-Sherren delayed treatment, and there are grounds for arguing that such a course would be wise also in childhood. I have not seen sufficient cases of this type to offer any advice. I think the present tendency is to operate as soon as the patients are fit, in order to remove the source of the peritonitis, the appendix, and to allow drainage from the most dependent portions of the abdomen. One must admit that it is impossible to drain the whole peritoneal cavity with one, or several, tubes, and that if such a patient survives one must be on the watch for localized abscesses in various parts of the belly, particularly the subdiaphragmatic spaces. One must also admit that the damage which operation is designed to avoid is already done in such cases, and it is probable that the original leak in the appendix is now sealed up. There is therefore a good argument for waiting, constantly on the lookout for localized collections of pus, which should then be drained wherever they may be. In these days of improved intravenous therapy, alimentary suction and antibiotics, such cases need no longer be hopeless.

### Post-Operative Treatment.

The average patient after routine appendicectomy requires very little after-treatment. Once the post-anæsthetic vomiting has subsided, liquids are allowed in full quantity and are followed quickly by light diet, then full diet. We no longer worry about whether the bowels have opened, though some surgeons begin to give paraffin or a similar mild laxative after two to three days, and others order an enema if the bowels have not opened by the fourth or fifth day. The patient may be allowed out of bed within a few days; but in a large ward it is more convenient to keep him in bed until a day or two before his discharge from hospital, usually from eight to ten days after operation. One caution is needed: it is wise to make sure that the bowels have opened at least once before sending the patient home.

Patients who have had a localized abscess carefully drained often go straight ahead with no further worries, although it is customary to give penicillin and often streptomycin or sulphonamides as well until they are obviously out of danger. I feel quite sure that patients with localized abscess, if treated conservatively, must cause more worry to all concerned than the patient who has had simple drainage as recommended. If any patient shows evidence of early ileus (abdominal distension, nausea *et cetera*), he is given fluids intravenously and nothing by mouth except sips of water to moisten the mucous membranes. Any patient with actual ileus, with repeated vomiting, is also treated by continuous gastric suction, by means of the intranasal or oral catheter or Ryle's type tube. I have already dealt with the management of the drainage tube, when one is used.

Patients with spreading peritonitis usually develop ileus before recovery. Obviously such patients require careful measurements of their fluid intake and output, and amounts which cannot be measured must be estimated. We have learned a lot in recent years about intravenous therapy, and it is a science in itself, but not the subject of this talk. Suffice it to say that the patient must have enough water, sodium chloride, Calories, protein and vitamins to keep him from going downhill. In the early stages this means that any previous deficit must be made up, allowance also being made for continued losses—for example, by gastric suction. In the later stages maintenance needs are sufficient. As soon as the patient is well enough fluids are allowed cautiously by mouth, and intravenous therapy is suspended as soon as the patient is able to take maintenance fluids by mouth. Such a state of affairs is usually preceded by spontaneous passage of flatus, soon followed by bowel actions. This usually occurs about the third to fifth day after operation.

So impressed am I by the results of the newer knowledge of fluid requirements that I am convinced that patients with peritonitis usually die because of altered biochemistry rather than from secondary shock, toxæmia or peripheral failure. When such a patient dies I now believe that it was because in our ignorance we have given either not enough or too much of some particular substance needed. We no longer seek to stimulate the bowels to work. Patients are given morphine in sufficient amounts to keep them at rest, and peristaltic stimulants are used only as a last desperate measure when a patient appears to be failing. Small repeated doses of "Prostigmin" or carbachol or equivalent drugs may in some cases just help a patient to turn the corner, but in simple paralytic ileus they are not usually needed.

Oxygen is useful in relieving abdominal distension which is largely due to nitrogen. Gas-gangrene antiserum is still used by some surgeons, but I do not think that it makes any difference to the prognosis, and I do not use it.

One might sum up the post-operative treatment in these complicated cases by stating that most of the patients with abscess and some of those with spreading peritonitis give very little worry and are obviously going to get better from the first day. Many have a certain degree of ileus and are a worry until bowel noises and flatus make their appearance, usually on the third or fourth day, or even longer. Those who are not obviously on the road to recovery by the fifth or sixth day must be suspected of having some complication.

### Post-Operative Complications.

Many post-operative complications are listed in the books, but few are of practical importance.

Post-operative pneumonia, if due to inhaled vomitus, may be serious and prolonged. Atelectasis and emboli may also required treatment.

Intraabdominal hæmorrhage should not occur if operative technique is careful. Massive hæmorrhage can be recognized and requires blood transfusion and reopening of the belly. Smaller hæmorrhages may go unrecognized, but may act as a nidus for infection and abscess formation.

Wound infection is seldom a worry if the wound is provided with a glove drain; if not, an abscess of the abdominal wall may require to be opened. Antibiotics have reduced the severity as well as the incidence of this complication.

With regard to fæcal fistula, I have seen an occasional persistent sinus, and assume that this means a foreign body of some sort—for example, a loose fæcolith. But cases of fæcal fistula after appendicectomy are rare. If drainage tubes are soft and are shortened daily, this should not occur. In the absence of intestinal obstruction the fistula will close spontaneously.

Pylephlebitis and portal pyæmia are things of the past. I have not seen a proven case. Perhaps penicillin and sulphonamides have prevented them.

Secondary intraabdominal abscess occurs most commonly in the pelvis, but is occasionally found in other sites after general peritonitis. It should be suspected if the patient is not progressing as well as expected, especially when abdominal distension and ileus persist. A raised temperature is not always present. However, leucocytosis is usually pronounced. A rectal examination every day or two will reveal the diagnosis in pelvic abscess. Tenderness and guarding elsewhere are useful signs, and in cases of subphrenic abscess plain X-ray films taken with the patient in the erect position are a help in diagnosis.

Secondary abscesses should not invariably be opened as soon as they are diagnosed. Many will be absorbed over a period of perhaps a week, and if the patient's condition is improving and the signs are decreasing one should wait.

These remarks apply particularly to pelvic abscess. If it enlarges, it will probably point in the anterior rectal wall and can be drained *per rectum* when fluctuation is certain. If it enlarges upwards, it will probably be possible to drain it through a small suprapubic wound without entering the unsoiled general peritoneal cavity.

Intestinal obstruction or secondary abscess or both together are the main causes of post-operative death in appendicitis with peritonitis. Early obstruction (from the fourth day onwards) may occur suddenly or may quietly supervene on paralytic ileus. Bowel noises return and the bowels are ready to work, but nothing happens. At operation many coils of small bowel in the neighbourhood of a drained abscess, or in the region of peritoneal soiling, are found matted together in a plastic adhesive "peritonitis", so-called. This can occur when there has been no evidence of peritonitis at the original operation. Talc used in preparing surgical gloves has recently been blamed as one cause.

It is difficult to decide whether to reoperate in such cases, and when one does so it is difficult to decide what to do. The immediate adhesions can be broken down and loops of bowel rescued from the angulation that occurs, but there is nothing to prevent the process from starting again. A simple ileostomy above the obstruction is recommended by some, condemned by others. The patients who die usually die from this cause. In theory it would be better to treat such patients by continuous Miller-Abbott suction, but in childhood it is often impossible to pass the tube down to the site. If the patient could be kept going long enough he should recover, because such plastic filmy adhesions are gradually absorbed and mostly disappear, and there is no frank pus and no danger of gangrene of obstructed loops. Nevertheless we nearly always operate and do not feel happy even after operation. I believe that this is our worst problem at present. I do not propose to deal with late obstruction by definite isolated bands. Uncomplicated paralytic ileus has been dealt with under post-operative treatment.

### Conclusion.

In conclusion, I should like to stress that the opinions expressed throughout this article, and particularly those concerning treatment, are my own responsibility and do not necessarily coincide with those of my surgical colleagues at the Royal Alexandra Hospital for Children. Nevertheless I have attempted to outline the usual present management of patients with acute appendicitis in this hospital.

### Summary.

1. In order that comparable groups of cases may be studied, it is essential that the classification of cases be detailed. A suitable classification is suggested, which includes nine subheadings.

2. It would appear that there is a satisfactory awareness of the disease and its dangers in childhood, on the part of parents and doctors in this city. Nevertheless the duration of symptoms prior to the patient's admission to hospital is still usually in the region of forty-eight hours, which is too long for safety.

3. Although rare under the age of one year, and uncommon in the second year, acute appendicitis is as common at the age of four years as at any later age. In the younger child the diagnosis is more difficult, and in fact in a large proportion of cases perforation occurs before the correct diagnosis is made.

4. The only constant symptom is abdominal pain, and the only constant sign is tenderness in the abdomen, or elicited *per rectum*. Both are extremely variable. Alteration in bowel habit is not commonly present. Nausea and vomiting are inconstant. For all practical purposes abdominal pain with tenderness indicates appendicitis unless some other diagnosis can be proved.

5. Not uncommonly acute enteritis leads to complicating acute appendicitis, which is particularly likely to be overlooked and to give rise to peritonitis.

6. There is but little tenderness when the appendix is hidden behind the caecum, or behind the mesentery of the small intestine, or in the pelvis. In these cases there is often an area of referred tenderness in the middle third of the right *rectus abdominis* muscle. Rebound tenderness is also a useful sign in a cooperative patient.

7. The position of the appendix is variable and is usually not noted by the surgeon unless the organ is fixed by adhesions or by its retroperitoneal situation. When a careful note is made in all cases at operation, a surprisingly large proportion of patients are found to have an appendix which cannot readily irritate the anterior parietal peritoneum, and which will not be readily accessible to the examining fingers on abdominal palpation.

8. In diagnosis, in childhood, it is particularly important to exclude medical conditions outside the abdomen which may produce abdominal pain and vomiting. The commoner problems in diagnosis are discussed. Diagnosis can usually be established on clinical evidence alone, but examination of the urine and a leucocyte count are often necessary. The state of the tongue and the smell of the breath are helpful.

9. Most of the surgical conditions which may confuse the diagnosis are considerably less common than appendicitis, and many can be adequately treated at operation for presumptive acute appendicitis. The most debatable of these is acute mesenteric lymphadenitis, which in my opinion is uncommon and should be diagnosed at operation only if all the mesenteric lymph nodes are considerably enlarged, and if the appendix is apparently innocent. Renal disease must be carefully excluded by suitable investigations.

10. Seven patients out of 2206 died, a mortality rate of 0·3%. Brief histories of each are given. The mortality rate in 49 cases with spreading peritonitis was 8·2%, and in 52 localized abscess cases 1·9%. Overseas figures in similar series are quoted for comparison.

11. Two of the deaths occurred after interval appendicectomy, one being an "anæsthetic" death. The other five all occurred in the under four years age group, and all these patients had at least a two-day history on their admission to hospital. In all fatal cases the appendix was retrocaecal, retroileal, or pelvic in position.

12. Urgent operation is recommended in all uncomplicated cases of acute appendicitis. My own views regarding exposure and technique in such cases are outlined. In the case of localized abscess in the right iliac fossa, drainage without appendicectomy is usually the safest procedure. The appendix should be removed several months later.

13. Pelvic abscess, if recognized before operation, or as a post-operative complication, may be treated on conservative lines. Treatment in such cases is outlined. Such abscesses, when ready, can be drained either *per rectum* or suprapubically, and appendicectomy can be postponed till later.

14. An appendiceal abscess discovered at operation—for example, retroileal or pelvic—may be opened, the pus sucked away and the appendix removed if this can be done without much manipulation of unsoiled areas. In such cases drainage through a separate stab-wound should be employed. The main incision should be provided with a glove drain down to the deeper layers. Conservative treatment in such cases is discussed but not recommended.

15. Patients with early general peritonitis require urgent operation, and the appendix should nearly always be removed. In really early cases it is safe to close the abdomen without drainage, but when there has been much soiling of peritoneum it is wiser to drain the pelvis, to guard against post-operative pelvic abscess.

16. Patients with established general peritonitis, with pre-operative ileus, may be moribund. They need pre-operative resuscitation. I have very little experience of such cases. There are grounds for advising conservative management, a constant lookout being kept for localized peritoneal pockets of pus, especially subphrenic and pelvic collections.

17. Post-operative management is discussed, including the use of antibiotics, gastric suction, intravenous therapy, and care of the bowels. It is considered that patients with peritonitis die from biochemical upset rather than from bacterial toxæmia.

18. The post-operative complications which are most to be feared are secondary intraabdominal abscess formation and obstruction due to plastic fibrinous adhesions of bowel loops. Management of these and other complications is discussed. Uncomplicated paralytic ileus will respond to adequate therapy.

### REFERENCES.


Aird, I. (1945), "Acute Non-specific Mesenteric Lymphadenitis", *British Medical Journal*, Volume II, page 680.

Gardner, C. E., junior, and Sapp, C. J. (1942), "Atypical Features in Manifestations of Acutely Inflamed, Nonruptured Appendix", *The American Journal of Surgery*, Volume LVII, page 477.

Jacobson, S. S. (1942), "Childhood Appendicitis", *American Journal of Diseases of Children*, Volume LXIII, page 1110.

Ladd, W. E., and Gross, R. E. (1941), "Abdominal Surgery of Infancy and Childhood".

Love, R. J. McNeill (1947), "The Appendix", H. K. Lewis and Company.

Oberhelman, H. A., and Austin, O. (1944), "Symposium on Abdominal Surgery; Peritonitis in Infancy and Childhood", *Surgical Clinics of North America*, Volume XXIV, page 93.

O'Connor, H. A. D., and Bessie, E. M. (1945), "Appendicitis; Survey of Last 2,000 Consecutive Cases", *New York State Journal of Medicine*, Volume XLV, page 1535.

Penberthy, G. C., Benson, C. D., and Weller, C. N. (1942), "Appendicitis in Infants and Children; 15-Year Study", *Annals of Surgery*, Volume CXV, page 945.

Stuckey, E. S. (1950*a*), "Recurrent Abdominal Pain in Childhood", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, page 827.

——— (1950*b*), "Appendicitis in Childhood", *Bulletin of the Post-Graduate Committee in Medicine in the University of Sydney*, Volume V, page 303.

Wells, A. Q. (1937), "Experimental Lesions of Rabbit's Appendix", *The British Journal of Surgery*, Volume XXIV, page 766.

Williams, H. (1947), "Appendicitis in the Young Child", *British Medical Journal*, Volume II, page 730.


## OBSERVATIONS ON ETHYLIDENE DICOUMARIN AS AN ANTICOAGULANT, WITH SPECIAL REFERENCE TO PUERPERAL PATIENTS.[1]


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THE first reports of the clinical use of dicoumarin (3,3′-methylene-bis (4 hydroxycoumarin)) were those of Allen and his associates at the Mayo Clinic in 1941. Numerous reports on the use of this drug have now made both its value and its limitations widely recognized, so that at the present time dicoumarin has become accepted as a useful addition to the growing list of drugs with a specific action.

In 1943 Fantl suggested the use of the ethylidene homologue of dicoumarin (3,3′ethylidene-bis (4 hydroxycoumarin)) as one which might give rise to fewer untoward hæmorrhagic reactions. He proved it to have certain advantages, namely: (i) it was less toxic than dicoumarin; (ii) the recovery from hypoprothrombinæmia was more rapid, being almost complete within twenty-four hours instead of three or more days after dicoumarin therapy; (iii) prolonged hypoprothrombinæmia could be achieved by continuous administration of the drug, which could be adequately controlled by regular estimations of the prothrombin level.

Burt, Wright and Kubik (1949) have suggested the value of another coumarin derivative (bis-3,3′ (4-oxycoumarinyl) ethyl acetate—"Pelentan" or "Tromexan") as an anticoagulant.

Kabat, Stohlman and Smith (1944), and Soulier and Guergan (1947) have reported that indandione derivatives will produce hypoprothrombinæmia, and the last-named, as well as Blaustein, Croche, Albenan and Richez (1950), have reported on the clinical use of phenylindandione.

No large series of results obtained when patients were treated with ethylidene dicoumarin has been assessed critically in the light of extensive experience. In the past two years ethylidene dicoumarin has been administered to patients at the Women's Hospital, Melbourne, and this report shows the value of the drug as an anticoagulant. During recent years pulmonary embolism had caused the death of three patients after Cæsarean section in just over 600 cases, while a further 12 patients had suffered lesser embolic complications. Hence it was decided to administer this anticoagulant to all such patients as a routine procedure, regardless of the reason for the operation. Thus the series includes the results obtained with such treatment in all cases of severe toxæmia of pregnancy in which increasing toxæmia indicated the necessity for operative interference.

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## EXPERIMENTAL INVESTIGATION.

### Method of Controlling Dosage.

Whenever possible a pre-operative level of prothrombin is determined in cases of elective Cæsarean section, but for emergency cases no special precautions are taken. The first dose of 500 milligrammes of ethylidene dicoumarin (obtainable in tablets containing 100 milligrammes) is administered as soon as the patient is able to swallow after operation, and a similar dose is given in twenty-four hours. On the third day 300 milligrammes are given, and further dosage is regulated by following the prothrombin level in the blood. At the outset an attempt was made to keep the prothrombin below 30% of the average normal level, but for reasons discussed below a level of 50% has been adopted in later cases.

The scheme of dosage after the first three days is based on the blood prothrombin level and is as follows: (i) prothrombin level below 20%, no ethylidene dicoumarin until the prothrombin level has been ascertained at the next test; (ii) prothrombin level between 20% and 30%, 100 milligrammes daily until the next test; (iii) prothrombin level between 30% and 40%, 200 milligrammes daily until the next test; (iv) prothrombin level between 40% and 60%, 300 milligrammes daily until the next test. Routine prothrombin tests are performed on Monday, Wednesday and Friday in each week, so that there is never a gap of longer than three days between estimations. Some special comments on this scheme of dosage are necessary. Because of the times fixed for routine prothrombin estimations, certain patients are tested after only twenty-four or forty-eight hours of ethylidene dicoumarin treatment and before its full effect can be determined; after this test it sometimes may be as long as seventy-two hours before another test is due. To cover this contingency it has been found both safe and effective to follow the routine first three doses with 200 milligrammes on the fourth and fifth days, and if another dose has to be given before the next test the dosage is reduced to 100 milligrammes. It is necessary to give ethylidene dicoumarin every day unless the level of prothrombin falls below 20%, and even then it is not wise to allow more than one day to elapse without treatment, since the prothrombin level usually rises above 50% very rapidly.

### Estimation of Prothrombin Level in the Blood.

The prothrombin level was estimated by a modification of Quick's method detailed below.

#### *Collection of Blood.*

Fresh oxalated blood taken under rigid conditions is used for all tests. The blood is taken into five-millilitre, dry, well-greased syringes and transferred to the receiving tube within one minute without air bubbles being present. Exactly two millilitres of blood are added to 0·22 millilitre of tenth molar potassium oxalate solution and quickly and thoroughly mixed. The specimens are taken immediately to the laboratory and stored in the refrigerator after being centrifuged. Estimations are made not longer than four hours later. If the plasma shows any hæmolysis or if any strands of fibrin or clot are present, the specimen is discarded.

#### *Method.*

*Reagents.*—Commercial rabbit's brain in ampoules containing 0·15 gramme obtained from Commonwealth Serum Laboratories is suspended in five millilitres of normal saline on the day of the test. This is mixed with five millilitres of one-hundredth molar calcium chloride solution originally standardized against silver nitrate. The mixture is heated in a water bath at 50° C. for fifty minutes. This treatment gives an active calcium thromboplastin mixture free from prothrombin. Since the results reported in this paper were obtained, a saline extract of human brain prepared as described by Toohey (1950) has been used continuously for twelve months. It has been found to be very satisfactory and is used in preference to the rabbit's brain preparation.

*Test.*—Plasma from three normal persons is first tested, and a curve for calculation of prothrombin time is prepared for the day's tests in the following way.

Plasma, 0·1 millilitre from each sample, is measured into each of two small agglutination tubes and placed in a water bath at 37° C. The active calcium thromboplastin mixture is incubated in the same bath. After two minutes 0·2 millilitre of calcium thromboplastin mixture is added to one tube, which is immersed in the water bath, and the time is taken from the addition of the thromboplastin until coagulation occurs. This procedure is repeated for each of the specimens. Plasma giving a clotting time of about eleven seconds is chosen for the normal control. Its prothrombin concentration is called 100%. The selected serum is diluted 1:2 and 1:4 with saline, and the procedure already described is repeated on each of these dilutions. A curve is then plotted from these results. The prothrombin present in the patients' specimens is now tested in the same way, concentrated plasma only being used. It is not advisable to test more than six samples at once, and in hot weather plasma should be kept in ice water before the actual test. The percentage of prothrombin is calculated from the curve which must be prepared for every batch of calcium thromboplastin mixture prepared during the day.

## RESULTS.

Routine prothrombin estimations were carried out on 453 patients who included 400 given ethylidene dicoumarin therapy as a prophylactic measure and 53 treated with ethylidene dicoumarin for some manifestation of thrombosis. Their subsequent clinical history has been correlated with the response to anticoagulant therapy.

### Prophylactic Group.

#### *Initial Prothrombin Level.*

There are 400 cases in this series in which ethylidene dicoumarin has been given as a prophylactic measure. In 364 cases the operation was Cæsarean section, and in the other 36 hysterectomy. Whenever possible a prothrombin estimation was made before operation; in most cases the level was more than 70%, but some apparently normal patients had a level as low as 50% to 60%. Although the latter patients were given the usual dosage, no undue drop in prothrombin level was encountered in any of them. In this series no initial prothrombin level fell below 50%, but it must be emphasized that most of the patients were women who had been able to carry a pregnancy to term, a fact which makes severe kidney or liver damage unlikely.

#### *Effect of Ethylidene Dicoumarin upon Prothrombin Activity.*

Fantl's experiments (1943, 1944) have shown that the fall in prothrombin level is not quite so fast after ethylidene dicoumarin administration as after ingestion of dicoumarin, nor is the level depressed for so long a period after the administration has ceased. These results were amply confirmed in our cases. In most instances the prothrombin level was less than 50% after seventy-two hours. In only one-eighth of the cases did it decrease to 20% or less.

If a dose of the drug was inadvertently omitted, there was invariably a sharp rise in prothrombin level in the next sample of blood tested.

#### *Maintenance Dosage.*

By the use of the scheme of dosage set out above it has been found that 234 patients (59%) required a daily maintenance dose of 200 milligrammes, 146 (36%) required less than 200 milligrammes on some days, while only 20 (5%) patients required more than 200 milligrammes daily. In none of the last-mentioned cases could the prothrombin level be reduced satisfactorily (Table 1).

#### *Duration of Treatment with Ethylidene Dicoumarin.*

The anticoagulant was administered in amounts sufficient to keep the prothrombin level below 50% until the patient was fully ambulant, which meant that in most cases

it was used for a period of ten to fourteen days. The bed exercises and early ambulation encouraged in the years previous to the use of ethylidene dicoumarin were still carried out.

*Clinical Findings.*

From the clinical point of view the results in the prophylactic group show that the treatment has been an unqualified success. No serious thrombotic complication has been seen during the period of anticoagulant therapy, although one woman developed a pulmonary infarct forty-eight hours after her last dose of ethylidene dicoumarin at a time when she was fully ambulant from a Cæsarean section and had been discharged from hospital earlier in the day. She responded normally to heparin and a further course of ethylidene dicoumarin. Four women with severe grades of varicose veins developed local thromboses in dilated and tortuous superficial vessels whilst taking ethylidene dicoumarin, in spite of the fact that there was a satisfactory reduction of the prothrombin level at the time when the thromboses occurred. The subsequent course of the thrombosed area was in no way different from that seen in other patients who were not taking an anticoagulant.

TABLE I.

*Correlation of the Numbers of Patients whose Prothrombin Level was Maintained below 50%.*

| Group. | Daily Dosage of Ethylidene Dicoumarin Required after Initial Dosage of 500, 500 and 300 Milligrammes on the First, Second and Third Days Respectively. | | |
|---|---|---|---|
| | 200 Milligrammes. | Less than 200 Milligrammes. | More than 200 Milligrammes. |
| *Prophylactic Group* (400 patients)[1]: (i) After Cæsarean section (364) .. .. (ii) After other pelvic operations (36). | 234 patients (59%) | 146 patients (36%) | 20 patients (5%) |
| *Therapeutic Group* (53 patients)[2]: (i) Femoral artery thrombosis (16). (ii) Calf vein thrombosis (14) (iii) Pulmonary infarction (12). (iv) Cardiac infarction (11). | 27 patients (out of 53) | 12 patients (out of 53) | 14 patients (out of 53) |

[1] Prothrombin level maintained below 50%, 83% of patients.
[2] Prothrombin level maintained below 50%, half the patients

Hæmorrhagic complications were remarkably few. No patients developed epistaxis or hæmaturia, nor was extensive bruising noted. The puerperal blood loss was normal in every respect. Two women who had an unexpected loss of blood *per vaginam* were cured by removal of portions of placenta; one of these was inadvertently maintained on ethylidene dicoumarin therapy, but there was no undue blood loss after operation. There was only one case of bleeding which appeared attributable to the use of ethylidene dicoumarin. In this case a severe loss occurred from the abdominal incision in a woman who had undergone Cæsarean section five days earlier. The bleeding was controlled by the intravenous administration of 50 milligrammes of vitamin *K* at three-hourly intervals three times. She also was given a pint of blood prior to removal of soft clot from the wound and resuture. At no stage had the prothrombin level fallen below 30%, but it is well recognized that undue hypoprothrombinæmia is not the sole cause of bleeding when this group of drugs is used.

One case of apparent idiosyncrasy to ethylidene dicoumarin has been noted. This occurred in a woman who developed a petechial rash forty-eight hours after Cæsarean section, and shortly after taking her second dose of 500 milligrammes of ethylidene dicoumarin. The rash was widespread on the trunk and arms, but no lesions in the mucous membranes were seen. There was also a slight rise in temperature. The rash faded during the next few days without the appearance of any new spots, and hæmatological investigation revealed no abnormality. Apart from this case, no untoward general manifestations were noted in any case in either this or the therapeutic group, so that ethylidene dicoumarin can be said to be virtually free from unpleasant side-effects.

All the mothers in this group have been encouraged to feed their infants at the breast. The babies were all given one milligramme of vitamin *K* shortly after delivery, a routine procedure not confined to these infants alone, and no bleeding occurred in any of the babies. Fantl and Nelson (unpublished work) have shown that little ethylidene dicoumarin is to be found in the breast milk of these mothers, so that it is safe for the babies to be suckled, although it is recommended that all such infants should be given one milligramme of vitamin *K* shortly after birth as a precautionary measure.

Brambel and Hunter (1950) have reported that ingestion of therapeutic doses of dicoumarol by 125 nursing mothers produced no effect on the prothrombin activity of the nursing infant, and clinically there was no evidence of hæmorrhagic manifestations in any of the infants. This last statement has been found to hold for 1500 other nursing infants of mothers given dicoumarol.

Included in this series are all the cases of Cæsarean section performed in a little more than two years. Many patients were submitted to this operation because of a toxæmia of pregnancy, which was not decreasing as the result of treatment. It is believed that liver damage is common in this type of patient, but in the few cases tested the prothrombin level was normal. As the operation was often decided upon suddenly, it was seldom that initial levels of prothrombin could be determined. In the early stages the ethylidene dicoumarin dosage was selected with care, but it soon became apparent that these women responded to the drug in the usual manner and that severe toxæmia was no contraindication to the use of ethylidene dicoumarin, with the possible exception of those women known to have chronic nephritis. There are eight such women in this series, and no special care was necessary to control their dosage.

In the whole group there were only 12 cases in which treatment reduced the prothrombin to a level as low as 10%. It has not been found possible to correlate this result with any common factor, and in none of them was there an untoward effect as the result of the low prothrombin level.

### Therapeutic Group.

Included in the therapeutic group are 53 patients, some of whom were treated privately by one of us (W.R.). The indications for giving an anticoagulant are set out in Table I, second section. The schedule of dosage was the same as for the prophylactic group, but the distribution of the maintenance doses necessary to keep the prothrombin level at 50% suggests that these patients require a slightly larger amount of ethylidene dicoumarin after the first three days. Thus 27 required 200 milligrammes daily, 12 required less than 200 milligrammes daily, but 14 required more than 200 milligrammes daily compared with only 20 out of 400 in the prophylactic group.

It is not proposed to present such small groups of cases in detail for comparison with cases in which dicoumarol treatment was given. The results were in no way inferior to our past experience when dicoumarol had been used in comparable cases, despite the fact that in the majority of the cases in this series it was decided to maintain the prothrombin at a level of less than 50% rather than at the previously recommended level of 20% to 30% (Rose, 1948). This point is discussed in detail later. One important fact emerges from the results obtained from this group of cases. There were six women to whom ethylidene dicoumarin was administered before term because of the development of thrombosis of a femoral vein, the earliest stage being the thirty-second week of pregnancy. One woman came into premature and somewhat precipitate labour while her prothrombin level was in the region of 30%, but her blood loss was normal. All the infants were

normal. This observation is of considerable importance in view of the work of Kraus *et alii*, who showed that in pregnant rabbits the administration of dicoumarol was capable of producing fœtal and maternal death. Their work was published at a time when we had already treated three patients without any trouble, so that we did not discontinue treatment in such cases. It would appear that in pregnant women, at least in the last eight weeks before term, it is safe to use ethylidene dicoumarin when clinical evidence indicates its necessity. However, we should like to suggest that ethylidene dicoumarin should not be used for thrombosis in varicose veins in the lower limb or the vulva either before or after delivery, as the results do not warrant its use in these conditions.

## DISCUSSION.

In order to assess the value of ethylidene dicoumarin, one needs to compare its action with that of dicoumarol, a well-recognized proprietary preparation—3,3'-methylene-bis (4 hydroxycoumarin). The largest series of patients to whom this drug has been administered comprises those reported by Allen and his colleagues at the Mayo Clinic. Our series is the largest group of patients treated with ethylidene dicoumarin so far reported. Both drugs bring about hypoprothrombinæmia, each taking between forty-eight and seventy-two hours to reduce the prothrombin level to what is regarded as a therapeutic optimum. Whilst dicoumarol maintains the prothrombin below normal for between three and seven days following cessation of treatment, ethylidene dicoumarin has the advantage that there is a speedy rise in prothrombin level in almost all cases once administration of the drug ceases, and within forty-eight hours normal levels are regained. This is a very real advantage, because it makes overdosage neither so likely nor so serious. When it comes to a consideration of efficacy, the figures in the prophylactic group in our series are in no way inferior to those reported for dicoumarol. In the therapeutic group no critical analysis of the results obtained is offered because the numbers are not large, but the results so far are indistinguishable from those obtained by dicoumarol therapy.

A consideration of the hæmorrhagic tendency of patients maintained on dicoumarol and on ethylidene dicoumarin is of interest. In our series of 453 cases there was only one example of blood loss which appeared to be due to the anticoagulant. Allen and co-workers (1947) reported that from their experience with dicoumarol one might expect minor bleeding in one case in every 25 and major bleeding in one case in 50 among post-operative patients to whom the drug was given prophylactically. On this evidence one should have seen 16 cases of minor bleeding and eight cases of major bleeding in our 400 prophylactic cases, whereas we experienced only one case of major bleeding and none of minor bleeding.

This is a point which requires more detailed consideration, because on the surface it makes a very telling factor in favour of ethylidene dicoumarin as a prophylactic and possibly also as a therapeutic anticoagulant. It will be recalled that the majority of our patients were maintained at a prothrombin level below 50%, whereas those of Allen were maintained at a prothrombin level between 20% and 30%. Thus our patients had a wider margin of safety in so far as bleeding complications are concerned. In our first 20 cases it was found far from easy to keep the prothrombin level constantly below 30%; but in spite of this two patients with femoral vein thrombosis had done quite as well as one could have hoped with a prothrombin level maintained lower, and it was thought that possibly the higher level might prove equally effective, yet be much safer. Thus it was decided to give the higher level a prolonged trial, and in our opinion the results have been just as successful as are those from cases in which levels below 30% have been maintained.

In a recent paper Brambel and Hunter (1950) state that the majority of puerperal patients showed a resistance to dicoumarol which necessitated large doses of the drug to affect the prothrombin time. However, when the prothrombin time did begin to change, it increased rapidly and had to be checked daily. A few patients were found to be hyperreactors to this drug. A comparison of these results with our own provides evidence that ethylidene dicoumarin is a more effective and safer anticoagulant for the prevention of post-operative thrombosis, particularly in puerperal patients.

The mode of action of these dicoumarin compounds is far from certain. That they do produce a fall in prothrombin level is beyond doubt, but in therapeutic doses they have no effect on whole blood coagulation time, such as is found with the use of heparin. However, other workers have shown that dicoumarol will prevent intravascular thrombosis on glass cannulæ, suggesting that there is an alteration in the clotting properties of the blood. Recently Gilbert and Nalefski (1949) have shown that dicoumarol can produce a prolonged rise in coronary flow volume greater than that seen after administration of xanthines. Bingham, Myer and Pohle (1941) reported that they had observed vascular dilatation when even moderate doses of dicoumarol were given. Thus some at least of the efficacy of the "anticoagulant" drugs may be related to vasodilator properties rather than to changes in the coagulation process in the blood-stream.

Certainly the present observations, that although the lowering of the prothrombin level has not always been optimal the clinical effects have proved satisfactory, could lend support to a theory that did not depend entirely on change in the clotting properties of the blood.

A further important point is one which has already received mention—namely, the question of the advisability of administering dicoumarin derivatives during pregnancy. Kraus *et alii* (1949) had found that when they produced severe hypoprothrombinæmia in rabbits during pregnancy, all the fœtuses and some of the mothers died; with smaller reductions in prothrombin level, but in the range that is usually regarded as therapeutically desirable, a few of the fœtuses were saved. As a result of these observations the following statement appears in a leading article in the *British Medical Journal* (1949):

> In the present state of knowledge it would seem wise to regard dicoumarol therapy as absolutely contra-indicated in pregnancy.

This suggestion is certainly not borne out by the results reported in this paper, to which we can add results from two further cases in which dicoumarol was given under the same circumstances. In all eight cases the mothers were examined after the thirty-second week of gestation, and all the babies were born alive and are known to be normal for at least the first few months of life. Three of these children are now over two years of age and healthy in all respects. Thus it would appear safe to give dicoumarin compounds in the last two months of gestation when there is definite clinical evidence such as the development of a femoral or sural vein thrombosis—an accident rarely to be seen in the early stages of pregnancy. Whether or not such treatment may be dangerous in the earlier months of pregnancy we are unable to say.

Early reports on the dicoumarin compound "Tromexan" were adverse, because large dosage (9000 milligrammes daily) was considered necessary and some deaths occurred after severe hæmorrhage following its use. However, Burt, Wright and Kubik (1949) have shown that after the initial high doses of 900 to 1200 milligrammes during the first two days the amount can be reduced to 300 to 600 milligrammes daily. The dosage must be controlled by daily estimations of blood prothrombin level until the desired level is reached, after which the estimations need be made on alternate days only, since the level is maintained steadily on a dosage of 300 to 600 milligrammes per day. In over 80% of patients given adequate dosage the prothrombin level of the blood was reduced to under 50% within thirty-six hours of commencement of the treatment, and it returned to over 50% within the same time after withdrawal of the drug. Some patients suffered slight nausea and vomiting, possibly owing to the bitter taste of the tablets, but no other toxic effects were noted.

From this report it appears that ethylidene dicoumarin has certain advantages over "Tromexan"—namely, lack of

taste which will cause nausea and vomiting, the need for control by prothrombin estimations only three times per week, and freedom from hæmorrhage following the suggested scheme of dosage.

Jaques (1949) has reported that the indandione derivatives have an entirely different mode of action from the dicoumarin compounds in the prevention of thrombus formation. They do not affect the blood prothrombin level, so that estimation of the blood prothrombin level cannot be used to indicate the amount of drug to be administered; neither can vitamin K be used to combat the effects of overdosage. Until there is more evidence to prove that this group of drugs can be administered with safety and that their effect is at least as satisfactory as that of ethylidene dicoumarin, the latter would appear to be the better drug for preventing the development of post-operative thrombosis.


## SUMMARY.

The amounts of ethylidene dicoumarin necessary to maintain the blood prothrombin at a suitable therapeutic level in post-operative patients and the method used for estimating the prothrombin level in the blood are reported.

From the clinical results obtained in 400 post-operative cases, 364 of which were of Cæsarean section and 36 of hysterectomy, treatment with ethylidene dicoumarin is shown to be safer and yet equally as effective as dicoumarin therapy.

The clinical results also show that ethylidene dicoumarin may be used in the last eight weeks of pregnancy without ill effect to either mother or child.



## ACKNOWLEDGEMENTS.

We wish to thank Dr. P. Fantl (the Baker Medical Research Institute) for his unstinted advice as to the simple and efficient modification of Quick's method for routine prothrombin estimations, and for information regarding other dicoumarin preparations as well as the indandione derivatives. Our thanks are also due to the hospital biochemists for the routine prothrombin estimations, and to the registrars for their cooperation in the treatment of the patients.


## REFERENCES.


Allen, E. V., Hines, E. A., Kuale, W. F., and Barker, N. W. (1947), "The Use of Dicoumarol as an Anticoagulant: Experience in 2,307 Cases", *Annals of Internal Medicine*, Volume XXVII, page 371.

Bingham, J. B., Meyer, O. O., and Pohle, F. J. (1941), "Studies in the Hæmorrhagic Agent 3,3'methylene-bis (4 hydroxycoumarin)", *The American Journal of the Medical Sciences*, Volume CCXII, page 563.

Blaustein, A. V., Croche, J. J., Alberian, M., and Richez, M. (1950), "Preliminary Report on the Clinical Use of a New Anticoagulant, Phenylindandione", *Circulation*, Volume I, page 1195.

Brambel, C. E., and Hunter, R. E. (1950), "Effect of Dicumarol on the Nursing Infant", *American Journal of Obstetrics and Gynecology*, Volume LIX, page 1153.

Burt, C. C., Wright, H. D., and Kubik, M. (1949), "Clinical Tests of a New Coumarin Substance", *British Medical Journal*, Volume II, page 1250.

Butt, H. R., Allen, E. V., and Bollman, J. L. (1941), "A Preparation of Spoiled Sweet Clover 3,3'-methylene bis (4 hydroxycoumarin) which Prolongs Coagulation and Prothrombin Time of the Blood: Preliminary Report of Experimental and Clinical Studies", *Proceedings of the Staff Meetings of the Mayo Clinic*, Volume XVI, page 388.

Editorial article (1949), *British Medical Journal*, Volume II, page 1279.

Fantl, P. (1943), "Inhibition of Blood Coagulation by Coumarin Compounds", *The Australian Journal of Science*, Volume VI, page 23.

——— (1944), "The Action of 3,3'-ethylidene-bis (4 hydroxycoumarin) as a Blood Anticoagulant", *The Australian Journal of Experimental Biology and Medical Science*, Volume XXII, page 125.

———, and Nelson, J. F., "The Secretion of 3,3'ethylidene-bis (4 hydroxycoumarin) in Milk", in the press.

Gilbert, M. C., and Nalefski, L. A. (1949), "The Effect of Heparin and Dicoumarol in Increasing the Coronary Flow Volume", *The Journal of Laboratory and Clinical Medicine*, Volume XXXIV, page 797.

Jaques, L. B., Taylor, E., and Lepp, E. (1949), "The Action of 2-phenylindandione-1,3", *Federation Proceedings*, page 81.

Kabat, H., Stohlman, E. F., and Smith, M. I. (1944), "Hypoprothrombinæmia Induced by Administration of Indandione Derivatives", *The Journal of Pharmacology and Experimental Therapeutics*, Volume LXXX, page 160.

Kraus, A. P., Perlow, S., and Singer, K. (1949), "Danger of Dicoumarol Treatment in Pregnancy", *The Journal of the American Medical Association*, Volume CXXXIX, page 758.

Rose, W. McI. (1948), "Anticoagulants in Clinical Practice", THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, page 549.

Soulier, J. P., and Guergen, J. (1947), "*Action hypoprothrombinéniante (anti-K) de la phényl-indandione étudiée expérimentalement chez le lapin. Son application chez l'homme*", *Comptes rendus des séances de la Société de biologie*, Volume CXLI, page 1007.

Toohey, M. (1950), "Prothrombin Estimation and Dicoumarol Therapy", *British Medical Journal*, Volume I, page 518.


# Reviews.

## HAIR.

IN "The Unconscious Significance of Hair", Dr. Charles Berg claims to show from the deep analysis of his patients and his interpretation of the hair habits and rituals of primitive peoples that there is a great deal more in this than meets the eye.[1] All normal behaviour has its real cause or source in endopsychic tension, and hair behaviour is an expression of affect attached to Œdipus, sexual and pregenital conflicts. The multitude of hair dressing establishments and the time spent on attention to the hair are evidence of the tremendous significance of the hair for women—and for men, too. Hair fetishism, as was suggested by Krafft-Ebing, arises from an infantile association between hair and a sexually desired object. The psychoanalyst goes much deeper and maintains that the fetish represents the phallus which the child discovered was missing in his mother. The bullrushes in the Moses story "are clearly" the maternal pubic hair. The long-haired Cavalier gratified his libido with wine and women, while the Roundhead whose hair style was a symbolic castration assumed a "compensatory aggression".

There are many other interpretations of habits and customs relating to hair which the reader who is not a Freudian will regard as fanciful. In his preface Dr. Berg asks: "Is, therefore, our self-expression in life and civilisation nothing more than a symptom identical in its source and mechanism with the symptoms of nervous and mental illness?" The recognition that "normal" and "abnormal" in human behaviour are matters of quantitative rather than qualitative difference is welcome in a book of this character.

We wish that Dr. Berg could have told us something about Bodgies and Widgies, who, we understand, may be known by their hair. The curious may note on page 49 a reference to the one word which the printers refused to print. Psychoanalysts will accept this work as a welcome addition to their literature and others will read it with interest and amusement, if sceptically. There is a short glossary at the end of the book for the enlightenment of the general reader.

## ROYAL NORTHERN OPERATIVE SURGERY.

THE first edition of "Royal Northern Operative Surgery" was published by H. K. Lewis and Company, Limited, of London, in 1939, and was reviewed in these columns. The comment was made that "this is not a book for either students or the occasional surgeon but for the trained surgeon in busy practice". This was because the subject matter attempted to traverse a very wide field, an intimate knowledge of both anatomical detail and surgical technique was demanded of the reader and descriptions of most operative procedures were very condensed.

The second edition,[2] 1951, recently received has done little to alter the impressions given in the first edition. There were eleven contributors as against seventeen in the new

[1] "The Unconscious Significance of Hair", by Charles Berg, M.D. (London), *D.P.M.*; *1951*. London: George Allen and Unwin, Limited. 9" × 6", pp. 112. Price: 15s.

[2] "Royal Northern Operative Surgery", by the surgical staff of the Royal Northern Hospital; Second Edition; 1951. London: H. K. Lewis and Company, Limited. 10" × 7", pp. 646, with 498 illustrations. Price: 90s.

edition which has an additional 83 pages and 35 new illustrations. There has been considerable rearrangement of some of the contents, and new chapters have been included on plastic surgery and neurosurgery. The latter is characteristic of the book as a whole as this important subject is covered in 36 pages, of which some eight and a half are taken up by illustrations, so that only a very limited field is covered in a very condensed style. Similarly, gynæcology is dealt with in 17 pages.

There is scope for further revision and exclusion of unusual and outmoded operative procedures, whilst more detail could be given of important techniques that really are the regular practice of the Royal Northern surgeons and which this book is supposed to portray.

The technique for dealing with parotid gland tumours has been rewritten and is much improved, but again lack of detail is regrettable.

Suprahyoid block dissection of the neck is still advocated for carcinoma of the lower lip and floor of the mouth. This disregards the important deep cervical glands. A brief account of Crile's dissection of the anterior triangle of the neck is given, but there is no indication as to when it is recommended.

In preparation for thyreoidectomy in toxic goitre, the use of methyl thiouracil is mentioned, but the time of one month for primary cases and two months for the secondary type to control toxicity and then two or three weeks of iodine medication is not in accord with modern practice, at least in Australia. For some strange reason the unnecessary and unsightly oblique lateral incision is still advocated for unilateral goitres and enucleation of an adenoma is advised instead of excision. No mention of total thyreoidectomy is made other than for "heart failure", in which it is of no value unless due to chronic thyreotoxicosis.

In discussing pneumotomy for hydatid cysts it is remarked "in a number of cases the cyst can be dissected free and removed". Also "when it has become infected the cyst has to be opened and the lining membrane treated with formalin", this showing complete ignorance of the pathology of this condition and of the accepted Australian teachings and practice.

The only procedure mentioned for reconstruction of the common bile duct is suture over a rubber tube, and one is not surprised to note that "there are occasional unhappy sequelæ of this operation".

Enough has been written to illustrate the many weaknesses of this book which, if the contributors had kept to their own individual techniques with exclusion of redundancies and possibly some little guide to immediate post-operative treatment, could have been made a worthwhile exposition of British surgery.

## A MEDICAL MANUAL.

"HOSPITAL STAFF AND OFFICE MANUAL", by Larkowski and Rosanova, presents a somewhat remarkable attempt by the contributors to compress into a small handbook the main outlines of everything medical.[1] To practitioners in busy metropolitan areas, as well as to those in isolated and remote places, it should prove very useful for immediate reference. As is stated in the foreword, the text is of novel quality, being short to the point of abruptness. This feature, however, is part of the general design of the manual, which is not intended to supplant or replace text-books, but to serve as a guide or reminder. The book contains brief accounts of almost every known disease and the appropriate treatment as well as accounts of diagnostic and therapeutic procedures. Methods of skin preparation and of operative technique are outlined and there is a wealth of information available in condensed form. The main headings are: routine technique, laboratory procedures, electrocardiography, X rays, X-ray technique, anæsthesia, *materia medica*, sulphonamide and antibiotic therapy, medico-legal aspects of medical practice, physiotherapy, medicine, surgery, urology, gynæcology, obstetrics, pædiatrics, orthopædics, dermatology, ophthalmology, otolaryngology, neurology and psychiatry. This little book is extremely well suited to its avowed purpose.

[1] "Hospital Staff and Office Manual", by T. M. Larkowski, M.D., F.A.C.S., and A. R. Rosanova, R.Ph., M.D.; 1951. Great Neck, New York: Romaine Pierson Publishers, Incorporated. 7¼" × 5", pp. 442, with many illustrations. Price: $4.95.

# Books Received.

*[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]*

"A Textbook of Clinical Neurology", by J. M. Nielsen, B.S., M.D., F.A.C.P.; Third Edition; 1951. New York: Paul B. Hoeber, Incorporated. 10½" × 7½", pp. 724, with 212 illustrations. Price: $10.00.

Designed to present the subject of clinical neurology in a form which may be used as a text-book during the medical course.

"Embryology of the Pig", by Bradley M. Patten; Third Edition; 1948. Philadelphia: The Blakiston Company. London: George Allen and Unwin, Limited. 9¾" × 6¾", pp. 366, with 187 illustrations, six in colour. Price: 35s.

An endeavour to set forth the fundamental facts of mammalian development.

"Joll's Diseases of the Thyroid Gland", by Francis F. Rundle, M.D., F.R.C.S.; Second Edition; 1951. London: William Heinemann (Medical Books), Limited. 10" × 7½", pp. 530, with 165 illustrations. Price: 84s.

A second edition of Joll's book first published in 1932, now largely rewritten by the present author.

"Major Symptoms in Clinical Medicine", by John Almeyda, M.R.C.P., D.P.H. (London), M.R.C.S. (England), with a foreword by Sir Adolphe Abrahams, O.B.E., M.A., M.D. (Cambridge), F.R.C.P. (London); Volume II; 1951. London: Henry Kimpton. 10" × 6½", pp. 344, with 137 illustrations, six in colour. Price: 25s.

Volume I was published in 1950 and reviewed in these columns in November of that year.

"Relief of Pain in Childbirth: A Handbook for the General Practitioner", by W. C. W. Nixon, M.D., F.R.C.S., F.R.C.O.G., and Shila G. Ransom, M.R.C.S., L.R.C.P., D.A.; 1951. London: Cassell and Company, Limited. 7½" × 5", pp. 116, with 12 illustrations. Price: 7s. 6d.

"The result of the opportunity for whole-time observation of a large number of patients."

"Mosquito Behaviour in Relation to Malaria Transmission and Control in the Tropics", by R. C. Muirhead-Thomson, D.Sc.; 1951. London: Edward Arnold and Company. 9" × 6", pp. 228, with 16 plates and 22 text figures. Price: 30s.

The purpose of the book is implicit in the title; the subject is covered in twelve chapters.

"The Essentials of Virus Diseases", by Patrick N. Meenan, M.D., D.C.P., Barrister-at-Law; 1951. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 268, with seven illustrations. Price: 20s.

Intended to narrow the gap between the practitioner and the laboratory and to make the student realize that the study of viruses is a science in its own right.

"Massage and Medical Gymnastics (Mary V. Lace)", revised by E. M. Tod, M.C.S.P., T.M.M.G., with a foreword by James Mennell, M.A., M.D., B.Ch.; Fourth Edition; 1951. London: J. and A. Churchill, Limited. 8½" × 5½", pp. 234, with 103 illustrations. Price: 16s.

The original author published the third edition in 1945; this, the fourth edition, is revised by E. M. Tod.

"Anæsthetics for Medical Students", by Gordon Ostlere, M.A., M.B., B.Chir. (Cambridge), D.A., with a foreword by C. Langton Hewer, M.B., B.S., M.R.C.P., F.F.A.R.C.S.; Second Edition; 1951. London: J. and A. Churchill, Limited. 7½" × 5", pp. 116. Price: 8s. 6d.

The book is "a dogmatic account of the elements of practical anæsthesia and analgesia", intended for house officers and junior resident anæsthetists. The first edition was published in 1951.

The Medical Journal of Australia

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## THE MEDICAL RESPONSIBILITIES OF SELF GOVERNMENT.

THE great and growing movement of nationalism is admittedly one of the leading features of the present age. When it is merely a determination to install self government and to be rid of domination from without, it is the most defensible and least harmful of national or racial aspirations, though even here a good case can be made out for foreign intrusion when the inhabitants of a country are unable, though willing, to make use of natural resources. Oil wells have lain undiscovered in countries like Mexico until British and American engineers and industrialists have exploited them for the benefit of the world as well as of the land in which they are situated. Nowadays Mexican citizens, mostly of Indian blood, have resented so much wealth, really a small fraction of the total earnings, going out of the country and particularly resent the direction of the industry having remained in non-Mexican hands. When nationalism is combined with ambitions of world domination it becomes one of the greatest menaces to our existing civilization. Just how violent can be the resentment at foreign domination is seen in the book by Pandit Nehru entitled "Glimpses of World History", now in a fourth and cheap edition. Pandit Nehru has had the advantages of an English education, in school and university, and is a man of wide culture and deep historical study, but that does not prevent a vehement partisanship appearing in his references to Britain. According to him British suzerainty in India has been one long record of exploitation, greed, tyranny and injustice. The only benefit he concedes to the Anglo-Saxon is the abolition of suttee, and here he affirms that the reform had already been inaugurated by Indian statesmen. Whether this book will lead to a rejoinder by British citizens possessing knowledge of India or whether it will be treated by them with silent contempt, is really no concern of ours and so need not be discussed; but we are deeply and personally concerned about the state of health in India and other countries seeking or in possession of self government; whether proper measures are being taken to prevent a native population from being a reservoir of diseases ready to spill out into other countries of the world, this aspect of the question being quite apart from humanitarian considerations concerning the inhabitants of the country being themselves endangered.

Closely linked with national health is national nutrition, for underfeeding, as we all know, invites and fosters disease. It is interesting to note that Pandit Nehru makes no mention in this latest book of his of the benefits of medical science and administration, or of the advantages of irrigation and mechanized farming. At present there are schools of medicine in India with high standards of instruction and examination, but these have arisen solely from British example and direction, and it is unfortunately only too true that this development has been seriously impeded by the hostility of the masses. Even today to the average Indian the hygiene of the white man is a nuisance; he wants to drink his holy sewerage; he will remove a proper antiseptic dressing and replace it by a crude mixture of cow manure and saliva; he will prefer his cataract to be couched by a thorn in the hands of a fellow native, even if total loss of both eyes is the result, rather than submit himself to the skill of an ophthalmic surgeon trained in western technique. Insistence on prophylactic or curative injections will still lead to riots, and the almost despairing hygienist will find his motives cruelly misrepresented and the measures he advocates bitterly opposed. As Kipling puts it:

> Take up the White Man's burden . . .
> The savage wars of peace . . .
> Fill full the mouth of Famine
> And bid the sickness cease;
> And when your goal is nearest
> The end for others sought,
> Watch Sloth and heathen Folly
> Bring all your hope to naught.

That an India breeding disease on a large scale can be a menace to the world is proved by the emergence of cholera from the valley of the Hoogli in 1817 and its spread in one fearful pandemic after another throughout the whole habitable globe with the exception of Australia. It is true that today, with our knowledge of its causation, cholera could not diffuse once more throughout the world making endemic foci, but there are viruses against which our defences are as yet primitive and which can readily develop perilous mutations amongst a large native population. Then again air travel has endowed spatial distance with temporal immediacy, enormously increasing the difficulties of adequate quarantine. Should India once more appeal to the world for assistance against famine or pestilence we may be certain that Australia will respond generously, but it is just possible that the help proffered would be coupled with the suggestion that a self-governing India should display self-help in agriculture and hygiene as well as in politics. Emphasis has been placed here on India, but actually the same argument applies to all countries which have achieved or are about to achieve emancipation from European or American control. All such countries must realize that their neighbours have rights. We find a model of this in freehold tenure of land in our Commonwealth. Ownership of land presents the possessor with an "aggregate of opportunities", as the economists of a former generation expressed it, but even in remote country districts there are restrictions to his liberty. He must not start fires capable of spreading, he must destroy noxious weeds, pests and vermin, if he keeps animals his fences must be beast-proof. The nearer his

property is to a highly populated centre, the more exacting are the limits to his freedom. His house must conform to certain architectural specifications, there are animals he is forbidden to keep, his sanitary system must be approved by an expert, the wiring in his electric lighting and power installations must be set up by a certificated technician, and so forth. These are not irritating infringements of liberty, no more so than the regulation of traffic by green and red lights in city intersections; they remind each citizen that he is not only a human but a co-human, and what protects his fellow man also protects him. The very same argument applies to nations, and chief amongst the responsibilities of each country towards the rest of the world is the war against disease. It has been jestingly said that China has no quarantine in her ports because no ship could bring into that country any disease which is not already well established. Let us see if complete independence or Soviet hegemony will improve this state of affairs. If the heavily populated countries close to Australia fail to come up to our standards of nutrition and health, then we shall be forced to tighten up quarantine regulations and to retain or even augment immigration restrictions. That will not be an economic or political question; it will be an urgent matter of national safety.

# Current Comment.

## PUNCH BIOPSY OF SYNOVIAL MEMBRANE.

IT is becoming increasingly fashionable to obtain minute specimens of tissue for examination with the minimum of inconvenience to the patient. Sternal puncture has long been recognized as of value in the investigation of obscure blood disorders, and needling of the liver and of the spleen, though undertaken less frequently and with more caution, has obtained general acceptance. The ingenious method devised by Ian Wood and his colleagues, in Melbourne, to obtain specimens of gastric mucosa for examination has proved very useful in the following of physiological and pathological changes, though its diagnostic application may be limited. Now members of the staff of the Mayo Clinic have produced an instrument and a technique for punch biopsy of synovial membrane, which obviate the usual operative incision and its attendant disability. The instrument, as described by its creators, Howard F. Polley and William H. Bickel,[1] has two main parts: first, a hollow, round stainless steel tube, five millimetres in diameter and twelve centimetres in length, with a trochar point and an ovoid opening near the point; second, a hollow tubular knife of the same material, which closely fits the lumen of the outer tube and has a sharp cutting rim. For punch biopsy of the knee joint (which has been its main use) a small stab wound is made over the medial or lateral aspect of the suprapatellar pouch at the upper level of the patella. Through this the instrument, with the inner tube fully inserted, is introduced and directed horizontally through the joint space. The inner cutting tube is then withdrawn sufficiently to open the aperture of the outer tube, tissue is engaged in this aperture with the aid of digital pressure, and the inner tube is reinserted, the engaged tissue being thus cut off. An average of two to four specimens is usually taken. These can be withdrawn for examination with a stylet. For the 130 procedures reported by Polley and Bickel, general anæsthesia and local anæsthesia were used 65 times each. No post-operative reaction or disability has been observed, and no restriction of the patient's subsequent physical activity has been found necessary. Polley and Bickel state that in eleven cases in which both punch biopsy and operative examinations were performed on the same joints, the specimen of synovial membrane obtained with the punch was as satisfactory as that obtained at operation; and M. B. Dockerty, speaking as a pathologist in a discussion of their paper, was enthusiastic over the possibilities of the new instrument. Of the 130 procedures sufficient synovial tissue was obtained for satisfactory histological and bacteriological examination from 112, and experience has increased the proportion of satisfactory results. Polley and Bickel do not suggest that punch biopsy will supplant exploratory arthrotomy in all instances. Arthrotomy may still be the procedure of choice when articular symptoms are suspected to be the result of mechanical alterations of function, and it may be necessary when punch biopsy cannot be used on the joint to be examined—practically all the satisfactory experience with punch biopsy reported has been on the knee joint, but it is not always so readily applied to other joints. On the other hand, when inflammatory or infectious articular disease is suspected in a joint suitable for the procedure, punch biopsy may be preferable. The simplicity of the procedure, the little inconvenience to the patient, and the useful information it has been found to provide, all suggest a useful role that experience will more clearly define.

[1] *Proceedings of the Staff Meetings of the Mayo Clinic*, July 18, 1951.

## ANIMAL AND VEGETABLE FOODS IN NUTRITION.

THE increasing difficulty in finding sufficient food for the effective nutrition of the peoples of the world makes an assessment of the relative values of foodstuffs from different sources—animal and vegetable—of particular importance. In an assessment of the relative values of foods from animal and vegetable sources, it is the nature of the protein which is of most interest. A seminar on the various aspects of the problem was recently held by the British Nutrition Society under the chairmanship of Professor R. C. Garry.[1]

Much has been learnt about the biological value of pure proteins from different sources and rather too much stress has been placed on these findings. We do not eat proteins as such; we eat food containing protein. Evidence is accumulating that the value of the protein may depend to some extent on the vehicle in which it is presented and in particular on the nature of the mixture of foods from different sources. In the long run the value of a protein depends on the amounts of the different essential amino acids it contains. In general the proteins from animal sources are nearer in composition to the proteins of the human body than are the proteins from vegetable sources, and individually are therefore of more value. Only soya bean meal, toasted to destroy the trypsin inhibitor it contains, is within the range of animal proteins. Vegetable proteins are usually poor in tryptophane and lysine, amino acids essential for growth. In a mixed diet great advantage can be secured by an appropriate mixture of proteins in different foods whereby a deficiency of an essential amino acid in one may be corrected by an excess in another. This is well illustrated by the observation that mixtures of animal proteins from meat or milk with those from cereals have shown a growth-supporting ability not inferior to that of animal protein alone. Cereals are well supplied with most of the essential amino acids, but are deficient in lysine, which is relatively abundant in the proteins of meat and milk. Another interesting example is the association of beef tea with toast. Beef tea, made directly from meat, has for many years been in disrepute as an addition to the food of invalids. Young rats fed on beef tea alone as the source of nitrogen do not grow, but soon die, but Chick and Slack have shown that when one-quarter of the necessary nitrogen was supplied by beef tea and the rest by white flour steady growth occurred at a rate greater than that when white flour supplied all the nitrogen. About 70% of the nitrogen in beef tea is in the form of gelatin, a protein lacking in both tryptophane and cystine, both of which are in satisfactory amounts in white flour. Gelatin, on the other hand, is rich

[1] *The British Journal of Nutrition*, 1951, Volume V, Number 2, page 243.

in lysine, an amino acid in which cereal proteins are notably deficient. Jellies and beef tea taken with toast or bread and butter can therefore be safely trusted to give convalescents a pleasant and nourishing snack.

The most impressive instance of supplementation between vegetable proteins is shown by mixtures of cereal proteins with those of the soya bean where the mutual advantage gained is great enough to produce a nutritive value comparable with milk proteins. Chick and Slack, working for the relief organization of UNRRA in Central Europe, found that a diet containing soya flour, malt extract and white flour, in which these ingredients supplied, respectively, 56%, 34% and 10% of the total protein, was about equal in growth-supporting value to a diet in which the same amount of total protein was provided entirely by milk. Much work has been done, particularly by R. F. A. Dean, in feeding children with this and similar mixtures. Nearly all the children with such mixtures, as a supplement in place of milk to a wholly vegetable diet, exceeded the standard gain in weight. Care had to be taken in the preparation of the food, for, if it was not heated sufficiently, the trypsin inhibitor of the soya bean interfered to some extent, and if over-heated, it caused diarrhœa. Sunflower seed is also being tried with considerable success in place of soya bean, but this is still in the experimental stage. The advantage of the sunflower is that it will grow readily in places where soya bean will not grow.

A purely vegetable diet, other than those mentioned, does not seem to be adequate as a source of protein for growing children. The disease, common in Africa among children, called kwashiorkor, or malignant malnutrition or fatty liver disease of infants, occurs in children whose diet is wholly of vegetable origin, predominantly carbohydrate. Here there is not only deficient protein but also deficiency of total protein. The addition of skim milk powder to the diet brings about rapid improvement. Part of the deficiency here may be of vitamin $B_{12}$, one of the early names of which was animal protein factor, for it is found in foods associated with animal proteins, but to a much less extent or not at all with vegetable proteins. The same disease is probably seen in all races of men, and Czerny's *"Mehlnährschaden"* is probably the same condition in European children.

There is still much work to be done before we can use available foodstuffs, particularly vegetables which are very much cheaper to produce than foodstuffs of animal origin, in the most efficient manner as sources of protein, but the work is well started.

## THE HEREDITY FACTOR IN EPILEPSY.

THE role of heredity in epilepsy is of some interest academically, but it is a matter of vital importance to the epileptic wishing to marry and have children. To the medical adviser the epileptic's questions on the subject can be perplexing. Despite emphatic opinions expressed in the past, an immediate "Yes" or "No" answer is seldom justified; but constructive and helpful advice should always be possible. The matter was considered at the annual session of the American Medical Association in 1950 in the light of the extensive experience of William G. Lennox,[1] and it is worth while to glance at the facts and views that he brings forward in his paper. His conclusions are based on evidence garnered from two groups: first, the 20,000 near relatives of approximately 4000 epileptic patients, and second, 122 twin pairs affected by seizures. Of the 20,000 near relatives, 3·2% had a history of seizures. The incidence was 3·6% if there was no evidence of brain damage prior to the patient's first seizure, and 1·8% if such evidence was present. These percentages have been calculated as, respectively, 7·2 and 3·6 times the incidence of epilepsy among draftees of the United States Army—a group reasonably representative of the general population. As additional evidence of a genetic factor in the ætiology of epilepsy, Lennox draws attention to the finding that in the group of epileptics with undamaged brain (essential epilepsy) the incidence of epilepsy among relatives decreased progressively with a later onset of seizures (7·6% if onset was in infancy; 1·5% if it was after the age of thirty years). Corresponding incidences for the group with brain damage (symptomatic epilepsy) were 2·9% and 1·3%. The findings from the 122 pairs of twins are particularly interesting. Among the twin pairs without evidence of prior brain damage, both co-twins were epileptic in 84% of cases of one-egg twins and in 10% of cases of two-egg twins. Among pairs with brain damage, the corresponding incidences were 17% and 8%. Among one-egg twins, concordance was usual not only with respect to seizures, but also with respect to the type of seizure and to the electroencephalographic pattern. Because of the importance to the epileptic of the maintenance of normal mentality, this question was investigated by examination of the intelligence quotients of 87 twin pairs. The results support the view that with mentality, as with convulsions, both heredity and acquired brain damage play important roles. The natural mental endowment of the patient is most important, and any gross anatomical impairment of the brain, especially if it occurs early, is of great influence. However—and this is, as Lennox points out, contrary to common medical opinion—the epileptic seizures themselves appear to play a distinctly secondary role in determination of mentality. "A good brain can 'take' a severe beating from epilepsy"—an important and encouraging piece of information for the clinician to have in mind when he talks to a patient (or parents of a patient) with good natural endowment and a brain not grossly damaged.

Lennox's discussion of the clinical significance of the genetic factor in epilepsy is practical and helpful. He points out that such a factor is no longer in question, but only its nature and extent. As to its nature, the fundamental transmission appears to be one not of epilepsy *per se*, but of a predisposition to epilepsy. As to extent, there is no reason to pillory epilepsy as a disease in which a predisposition is unduly conspicuous. It is probable that a transmitted predisposition is greater for many common medical conditions than it is for epilepsy. The hereditary factor in epilepsy appears to be about the same as that in diabetes, one-half that in obesity and one-eighth that in migraine, yet "no state has as yet forbidden migrainous persons to marry". Unjustified discrimination, and the fear from which it arises, should be reduced by the success of present-day therapy of seizures.

Advice to be given to epileptics wishing to marry and have children is essentially an individual matter and cannot be standardized. All aspects of the potential parents' physical and mental make-up come into the picture. Lennox summarizes the conditions that minimize the likelihood of the birth of an epileptic child as follows: a family history devoid of epilepsy or migraine for the spouse, as well as the patient, and minimal abnormality of their electroencephalograms; some acquired condition that is at least partially responsible for seizures; late onset of the illness, and a normal mental endowment. It is obvious that there will be cases in which prospective parents should be discouraged; others need to be encouraged. Persons are "carriers" of not one, but a great many, qualities. These transmitted traits, it is pointed out, determine, or help to determine, not only physical structure and physiological function of the body, but also the even more important characteristics of intelligence, personality and social consciousness. A person's intellectual and social assets may outweigh his physical liabilities. This emphasis in Lennox's paper on the aspects that allow for encouragement of prospective parents is rather unusual and may arouse criticism. However, quite apart from Lennox's own standing and the magnitude of his investigation, the thought contained in the last sentence of his paper is most significant: "Unfortunately, persons who should be encouraged are the ones most alive to their social responsibilities and most likely (unless advised otherwise) to forego parenthood." Unnecessary encouragement is unlikely from any source, but the possibility of unnecessary discouragement is real.

[1] *The Journal of the American Medical Association*, June 9, 1951.

# Abstracts from Medical Literature.

## SURGERY.

### Chloramphenicol and Aureomycin in Surgical Infections.

W. A. ALTEMEIR AND W. R. CULBERTSON (*The Journal of the American Medical Association*, February 17, 1951) discuss chloramphenicol and aureomycin therapy in surgical infections. They state that the range of these two antibiotics is very similar; Gram-negative aerobic bacilli, bacterioides, Gram-positive pyogenic cocci, clostridia and certain viruses and rickettsia were sensitive to each agent. Penicillin is more effective against Gram-positive pyogenic cocci, staphylococci and streptococci as a rule. An investigation showed, however, in a series of cases that hæmolytic streptococci were more readily overcome by chloramphenicol and aureomycin than by penicillin. Mixed infections with Gram-positive and Gram-negative organisms seemed to respond best to chloramphenicol and aureomycin. The combination of penicillin with one or other of these preparations was often effective in surgical cases. Resistance to aureomycin and chloramphenicol developed in about 10% of cases.

### Cancer as a Sequel to War Wounds.

LEON GILLIS AND STANLEY LEE (*The Journal of Bone and Joint Surgery*, May, 1951) present a series of 24 cases in which a squamous carcinoma has arisen at the site of old war wounds; of the patients concerned, at least 13 have died of cancer. The authors point out that a patient with a chronic discharging sinus or an extensive adherent scar is never safe from the risk of malignant change. Examples are still occurring more than thirty years after the end of the first World War. The possibility should be kept in mind by those concerned with the long-term treatment of wounds of this kind. Reasonable prophylactic measures would be excision of adherent or unstable scar with, if necessary, replacement by suitable pedicle flaps having a good blood supply, and earlier amputation if an osteomyelitic sinus persists for several years and does not yield to treatment. Supervision in doubtful cases should be frequent and should not be relaxed with the passage of years. Warty changes or indolent ulceration of scars should be regarded with grave suspicion and investigated by biopsy. Any increase in pain or discharge in association with a sinus should receive prompt attention. Finally, if malignant change supervenes, treatment should be as speedy and as radical as with any other cancer.

### Megacolon.

R. B. HIATT (*Annals of Surgery*, March, 1951) denies the theory of Hirschsprung, formulated in 1888, that the hypertrophied colon is the primary site of the disease. He states that after taking a series of pressure readings in the distal part of the colon and rectum and serial sections through these portions of the intestines, he decided that the failure of forward propulsive contractions, associated with great diminution or absence of the autonomic ganglion cells of Auerbach's plexus, was the basic abnormality. When the peristaltic reflex reaches the recto-sigmoid region it enters a syncytium of nerve fibres in which there is no ganglionic control. The gut here not only is incapable of progressive peristalsis, but also is kept in a tonic state by the muscle itself. The hypertrophy and dilatation of the proximal segment are the reaction to the functional obstruction of the achalasic bowel. Sometimes the reduction in the ganglion cells extends for some distance into the hypertrophied segment, and in these cases it may be impossible to tell how much of the bowel should be resected. It is in this type of case that surgical failure is possible. The author discusses the dangers of hypotonic enemata in these cases, as leading to acute and sometimes fatal water intoxication, and recommends the use of isotonic enemata. He states that there are three main clinical types of this disease: the most common, in which the dilated and hypertrophied segment ends abruptly just above the recto-sigmoid junction, a second much less common group, in which the transition is more gradual, and a third form, in which there is a megarectum as well as a megacolon. He describes a modification of Swenson's operation for removal of the non-propulsive section of the rectum down to the anus. This is essentially the intussusception of the rectum and sigmoid colon through the anus and then the anastomosis of the sigmoid colon to the anus. The presacral space is drained through the perineum.

### Radical Mastectomy.

D. H. SPRONG AND W. F. POLLOCK (*Annals of Surgery*, March, 1951) stress the facts that the female breast is the most common site of cancer, and that cancer of the breast occurs in almost 4% of adult women. After a short review of the historical development of radical mastectomy, they discuss the amount of skin removed and the preparation of the skin flaps, the treatment of the pectoral muscles and the axillary dissection. Figures are quoted showing the diminution in survival rate if the *pectoralis minor* is preserved and linking the survival rate to the number of lymph nodes removed, the varying skills of different surgeons and the length of time taken for the operation. The authors state that they support the "criteria of categorical inoperability" published by Haagensen and Stout—(i) development of the carcinoma during pregnancy or lactation; (ii) extensive œdema of the skin over the breast; (iii) satellite nodules in the skin over the breast; (iv) intercostal or parasternal nodules; (v) œdema of the arm; (vi) proved supraclavicular metastases; (vii) carcinoma of the inflammatory type; (viii) distant metastases; (ix) the presence of any two of the following: ulceration of the skin, limited skin œdema, fixation of the tumour to the chest wall, axillary nodes more than 2·5 centimetres in diameter and proved by biopsy to be carcinomatous, axillary nodes fixed to skin or deep structures and proved by biopsy to contain carcinoma. They state that there is general agreement on these, though Brooks and Harrington maintain that radical mastectomy for the acute carcinoma of pregnancy and lactation still gives better results than any other method of treatment. They discuss in detail the contentions of McWhirter and on statistical and other grounds deny them all, and they emphasize various deficiencies in his reports. They further state that if irradiation is the only form of treatment, then the five-year survival rate is 21% to 25%, which is essentially the same as the survival rate for untreated breast cancer, and conclude that irradiation is not an adequate substitute for axillary dissection.

### Aureomycin in Surgical Infections.

A. M. RUTENBURG, F. B. SCHWEINBURG AND JACOB FINE (*Annals of Surgery*, March, 1951) survey the use of aureomycin in 263 cases. They state that it was found to be of considerable value in controlling the normal intestinal flora, in sterilizing the infected urinary tract, in the control of peritonitis when it was usually used in conjunction with penicillin, in the control of biliary infection and in miscellaneous surgical infections. The organisms found most frequently to be resistant were *Pseudomonas aeruginosa*, *Proteus vulgaris* and an occasional strain of *Escherichia coli*. It was ineffective in the presence of a localized abscess. The drug was administered in the following ways: (i) Orally. A dosage of 0·5 gramme was given six-hourly. (ii) Intramuscularly. A dosage of 240 to 400 milligrammes per day was given in three or four doses, the drug being dissolved in procaine solution. This method has largely been discontinued. (iii) Intravenously. A dosage of 600 to 1000 milligrammes per day was given in two doses, the aureomycin being buffered with sodium glycinate in 500 millilitres of isotonic glucose solution. Some gastro-intestinal symptoms (nausea 13%, vomiting 6%, diarrhœa 2%) occurred in association with the oral administration. Thrombosis of the vein usually supervened after two to four intravenous infusions of the drug. In two patients of the 30 tested the prothrombin time was prolonged, but no case of undue bleeding was encountered. However, the authors suggest that vitamin *K* should be given simultaneously with the aureomycin. In an addendum they note the occurrence of severe diarrhœa associated with severe spasm and a membranous type of inflammation in the colon. Several cases have occurred of stomatitis and œsophagitis with dysphagia, substernal pain and burning lasting for several weeks.

### Cystic Hygromata of the Neck.

KENNETH C. SAWYER AND ROBERT WOODRUFF (*Archives of Surgery*, July, 1951) present a paper on cystic hygromata of the neck, basing it on experience with eight patients. They state that cystic hygromata are benign, multilocular, cystic tumours of lymphatic origin with a lining of endothelium. The explanation of these growths is related to Sabin's theory of the development of the lymphatic system. A capillary plexus is formed from each jugular vein during the primary stage of development. Portions of these plexuses break off, and from these segments, the jugular sacs develop on each side. This development is the beginning of the lymphatic system. Through some anomaly of growth, accident or fibrosis, portions of the jugular sacs fail to establish a communication with the venous system. Hence, free areas of lymphatic tissue which retain the inherent property of growth and penetration exist in the cervical region. Goetsch also demonstrated that hygroma cysts arise primarily from membranous sprouts

derived from the walls of cystic spaces which are already present. These sprouts penetrate and permeate into the corresponding tissues and eventually become canalized and form additional cysts. Four of the authors' eight cases were in children, the remainder in adults. It is stated that the neck is the commonest site for hygroma formation, but occasionally the tumours develop in the retroperitoneal tissue, groin, popliteal space and axilla. Diagnosis is not difficult, but they must be differentiated from branchial cleft cysts, thyreo-glossal cysts, lymphomata and secondary metastatic cervical neoplasms. For treatment, the authors recommend surgical incision as soon as possible. They do not favour aspiration or incision and drainage, as permanent relief is not afforded and secondary infection has been a serious and even fatal complication. While expectant treatment is occasionally followed by recession of the growth, the probability of rapid growth or reappearance after recession makes such conservatism unwise. The authors are not impressed with irradiation treatment, as mature tissue of this nature is inherently radioresistant, and it is difficult to expect any effect but some fibrosis from irradiation. Injection with a sclerosing agent followed by surgical removal in three to six weeks has been advocated by some. However, the authors' experience leads them to believe that complete excision must be carried out to avoid recurrence. Patients operated on shortly after the discovery of the tumour were found to have thin-walled cysts confined to contiguous fascial spaces, and these growths were removed without difficulty. On the other hand, in cases in which there had been delay, the lesion had progressed and invaded the surrounding tissues. At operation, instead of a well localized thin-walled cyst, a thick-walled invasive lesion was encountered; this had permeated extensively, engulfing nerves, blood vessels and other vital structures. Five of the authors' eight cases illustrate this point.

### Acute Pancreatitis.

JOHN BRINKMAN AND HYMAN ROSENFELD (*The American Journal of Surgery*, December, 1950) present a study of 25 patients with acute pancreatitis admitted to a large city hospital from 1943 through 1947. They state that the most useful clinical and pathological classification of the condition is that of two types, the simple acute œdematous form and the acute pancreatic necrosis or hæmorrhagic form. In the series discussed the latter form was less common, but much more severe in the clinical picture and course. The patients varied in age from fifteen to seventy-one years, the majority being between thirty-five and sixty years of age. The symptomatology was very variable, but only two of the patients were admitted in evident shock. Symptoms and signs were so varied that perforated ulcer, intestinal obstruction, acute biliary disease, mesenteric thrombosis, kidney colic, acute appendicitis, alcoholism and acute gastro-enteritis were among the admitting diagnoses in this series. The serum amylase estimation was the most useful laboratory test; it was the basis of the diagnosis for ten patients not operated on. Of the 25 patients, 15 were operated on, mainly because the diagnosis was obscure. There were four deaths in the group operated on and only one death in the group not operated on, that of a woman with a two weeks' history of symptoms, who was not in a fit condition for surgical operation. She had a large subphrenic collection in the right side with a pronounced pleural effusion. All the patients who were operated on and were admitted to hospital early recovered. It is considered that the findings confirm the opinion that conservative treatment is the treatment of choice, provided suppuration has not occurred. Conservative treatment consisted of the elimination of food intake by mouth, the intravenous administration of saline, glucose, blood, plasma and "Amigen", chemotherapy and oxygen therapy.

### Spigelian Hernia.

E. ERIC LARSEN (*The American Journal of Surgery*, July, 1951) reports an instance of Spigelian hernia. He states that herniation through the *linea semilunaris* is little understood and infrequently recognized. It may assume importance in the differential diagnosis of some abdominal tumours or as a cause of intestinal obstruction. In this case, careful and prolonged studies failed to reveal the true nature of the condition, which simulated an intra-abdominal mass in the left lower quadrant of the abdomen until a laparotomy was performed. The hernial opening was situated in the left *linea semilunaris* at the semicircular line of Douglas—the point where the posterior layer of the rectus muscle ceases.

### Thoracoscopic Sympathectomy.

E. KUX (*Diseases of the Chest*, August, 1951) has performed exeresis of the thoracic part of the sympathetic trunk in more than 500 patients with the aid of the thoracoscope. In the treatment of duodenal ulcer and in carefully chosen cases of *angina pectoris* the results were excellent. It was used also in the treatment of hypertension, eliminating the risk of the open operation. A very good view of the sympathetic trunk could be obtained through the thoracoscope from the caudal portion of the inferior cervical ganglion down to the diaphragm. Even the branches and the *rami communicantes* could be seen in rich contrast and detail with the endoscopic illumination.

### Lye Strictures and Cortisone.

N. ROSENBERG, P. J. KUNDERMAN, L. VROMAN AND S. E. MOOLTEN (*Archives of Surgery*, August, 1951) state that it has been demonstrated that cortisone inhibits granulation tissue formation in experimentally induced wounds, owing probably to a local inhibitory action of the hormone on fibroblasts. With a view to the practical application of these data to man in the prevention of cicatricial stenosis of the œsophagus following injuries such as lye burns, the authors conducted experiments on rabbits. Under direct vision, through an infant-sized œsophagoscope, the œsophagus of a number of rabbits was burned with 5% sodium hydroxide solution. Cortisone was administered subcutaneously in doses of six to ten milligrammes per kilogram of initial body weight, with gradual reduction in dosage after the first two weeks and withdrawal after the fourth week. The results in 26 rabbits are summarized as follows. Seven of the eight control rabbits which survived longer than sixteen days presented well-defined, localized strictures of the œsophagus. In the cortisone-treated group only one of the seven rabbits which survived the initial period after injury developed significant narrowing of the œsophagus. In this animal stenosis was slight and far less than in the controls. In the animals treated with cortisone a much higher incidence of complications was seen. However, cortisone, by inhibiting fibroplasia, greatly diminishes the tendency to scar tissue contracture in the œsophagus after such an injury. The authors are continuing the experiments to test the effects of delayed administration of cortisone on sodium hydroxide burns of the œsophagus with a view to taking advantage of normal defensive reactions to injury in the interval before irreversible fibroplasia develops. A duplicate series of observations with ACTH is being carried out.

### Water Diuresis and Ureteral Peristalsis.

G. FALK AND J. A. BENJAMIN (*Surgery, Gynecology and Obstetrics*, August, 1951) state that evidence gathered from histological findings, determination of glomerular filtration rates and renal clearances all point to functional immaturity of the kidneys at birth. They report results of an investigation undertaken in an infant with complete exstrophy of the bladder to obtain quantitative information on water diuresis and to study the contractions of the ureters during the diuresis. The method of investigation is given in detail, and the authors conclude that water diuresis was found to reach adult levels by the end of the first year of life. They state that the rates of urine flow in this infant at the age of one year exceed those reported for an adult man, when the values are compared on the basis of surface area and body weight. This suggests the possibility that infants at this stage of development may normally have higher rates of output than adults. An increase in urine flow produces an increase in the frequency and amplitude of ureteral contractions.

### Hand Infections.

IAN GORDON (*The British Journal of Surgery*, January, 1951) advocates a conservative attitude in the treatment of infections of the hand. He recognizes clinically only pulp infections and flexor cellulitis, and under the latter heading groups all infections involving the soft tissue overlying the flexor aspect of the proximal two phalanges, including infections of the flexor tendon sheath. He states that the principles of treatment of hand infections have been based on the teaching of Kanavel; these were that barriers of spread were largely anatomical, that incision should be early, even before pus had formed, and that incisions for sheath infections should be placed laterally. The author criticizes these principles, especially that of early intervention. He bases his conclusions on a large series (over 2000 hand infections). His method of treatment consists in the administration of large doses of penicillin (250,000 to 1,000,000 units twice daily), rest and dry packing with kaolin. If localization occurs and pus points, the skin is snipped away and the slough picked out if possible, a clean granulating cavity being left in the depths. Healing time has not been extended by this method, and final function has been good. Tabulated results are appended.

# Special Article.

## EPIDEMIC HÆMORRHAGIC FEVER OR RYUKOSEI SHUKKETSU NETSU.

EPIDEMIC hæmorrhagic fever, or *ryukosei shukketsu netsu*, a disease unknown to the western world, has made its appearance among United Nations troops serving chiefly in the central sector of the Korean front. The disease first broke out early in July, 1951, and continues until the present time.[1] There have been 200 cases to date, with a mortality rate of approximately 12%.

The Japanese first came into contact with this disease in the Songo district of Northern Manchuria in 1939, when an outbreak occurred among their troops in this area. It was then given the name of Songo fever. It was unknown to them in either Korea or Japan. After subsequent outbreaks among their troops in other parts of Manchuria, it was formally recognized in 1942 as a clinical entity by the Medical Department of the Japanese Army. It was then established that several outbreaks of an undiagnosed fever among their troops in the years 1935 to 1938 in northern and north-eastern Manchuria must have been the same disease.

Although there has always been traffic between Korea and Manchuria, and although United Nations troops passed through this area last October, there were no known cases at that time. Therefore it would appear that the disease has been introduced from Manchuria into Korea by the Chinese Communist Forces, who did not enter the war until November, 1950. The Japanese make no mention of this disease as having occurred among the local Chinese in Manchuria, though they mention having heard reports of similar disease occurring across the Siberian border. To date no enemy prisoners of war have been taken suffering from the disease.

Epidemic hæmorrhagic fever is said to be transmitted by the mite *Lælaps Jettmari Vitzthum*, the field rodent *Apodemus agrarius* being the host of the mite and the probable reservoir of the disease. *Apodemus agrarius* is common throughout Korea as well as Manchuria. The Japanese think that the body louse may also be a vector.

The incubation period appears to be from one to two weeks, and no eschar as in scrub typhus is apparent. The onset is abrupt, the illness commencing with general malaise, chills, severe headache, and generalized aching of the limbs followed by high fever, vomiting, thirst and prostration, in severe cases the patient being semicomatose; the temperature rises to a peak of 104° F. to 105° F. within forty-eight hours, the pulse rate is not unduly raised, and severe conjunctival hæmorrhages occur, the conjunctiva in some cases being so intensely red that no white is visible. The face takes on a characteristic puffiness; a petechial rash appears on the axillary folds, and in some cases on the abdomen and thorax. The tourniquet test produces a positive result, and any trauma may cause ecchymosis. The cervical and axillary glands become enlarged and tender. Hiccup may become very troublesome and vomiting severe. Hæmorrhage from the gums and epistaxis are common; low back and testicular pains occur, also photophobia and blurring of vision, and insomnia with nightmares. Abdominal pain, chiefly in the upper quadrants, is common, the liver and spleen becoming slightly enlarged and tender in some cases. Jaundice is rare and only very slight when it occurs.

Oliguria is present during the acute stage, the urine containing albumin (up to "++++"), red blood cells (up to frank hæmaturia), and granular and hyaline casts.

The hæmorrhagic diathesis may affect any organ or system. In severe cases hæmoptysis, hæmatemesis and bloody diarrhœa occur. If the brain is involved, delirium and coma may result. The blood pressure is reduced. If dyspnœa and cyanosis supervene, the patient dies from fulminating hæmorrhagic pneumonia.

The blood picture is as follows. The number of erythrocytes and hæmoglobin value are normal. Investigation of the white blood cells reveals leuchæmoid leucocytosis, the number averaging 30,000 to 40,000 per cubic millimetre, and the highest number being 100,000 per cubic millimetre. Slight relative neutrophilia is present with a "shift to the left", and myelocytes and myeloblasts are present. Neutrophile cells number 70% to 80%, lymphocytes number 15% to 20%, monocytes number 5% to 10%, and eosinophile cells are absent. Of the lymphocytes, 25% are atypical. In a number of cases the platelet count is slightly reduced. The coagulation and bleeding times are within normal limits. After the first week the erythrocyte sedimentation rate is slightly increased. The non-protein nitrogen content of the blood is increased to 60 to 80 milligrammes *per centum*. The Weil-Felix test, the Widal test and the Wassermann test all produce negative results. The icterus index and the thymol turbidity are normal. The cerebro-spinal fluid is under normal pressure and occasionally contains red blood cells.

The temperature falls by rapid lysis to normal on the sixth or seventh day. Coincidently with the disappearance of the fever there is an increase in the severity of the clinical symptoms and signs—*lysis paradoxus*.

Recovery commences during the second week, and death, when it occurs, takes place one or two days after the temperature falls.

The prognosis is difficult to estimate; some acutely ill patients have recovered, and others mildly ill have died in a short time.

As recovery takes place, a sudden diuresis occurs, with recovery in the concentrating power of the kidneys. Full recovery takes place in three weeks, except when the patient has a past history of renal disease.

Complications include parotitis, orchitis, pancreatitis, hepatitis and encephalitis.

Death is associated with hæmorrhages in various organs, the chief sites being the pituitary gland, the gastro-intestinal tract, the lungs and the kidneys. One patient died of a ruptured spleen.

*Post mortem* the kidneys are found to be involved in all cases; the cortex is œdematous and pale, the medulla is dark red and hæmorrhagic, and the collecting tubules are loaded with albumin and casts.

At first it was thought that this disease was leptospirosis, as the symptoms and signs were rather similar; all patients gave a history of bathing in the rivers and streams, and spirochætes were isolated from the kidneys of field rodents collected in the areas from which the patients came. However, no spirochætes could be demonstrated in the patients' blood or urine under dark-field illumination, and none were revealed in post-mortem specimens by silver staining. Attempts to grow the spirochætes in culture were unsuccessful, and agglutination tests gave negative results. Doubt was then cast on the diagnosis. Japanese doctors who examined some of the patients and post-mortem specimens said that the disease in their opinion was epidemic hæmorrhagic fever.

Treatment is symptomatic, with supportive sedation. Blood transfusion and the intravenous administration of 10% glucose solution in water with added vitamin *K* and vitamin *C* are employed. The transfusion of 250 millilitres of blood from patients in their third week of convalescence appears to be of value. Penicillin, streptomycin, aureomycin, "Chloromycetin" and terramycin were all tried without the slightest effect.

The commonest diseases to be considered in the differential diagnosis are leptospirosis, epidemic typhus, scrub typhus, relapsing fever, hæmorrhagic smallpox and the purpuras.

To summarize, epidemic hæmorrhagic fever is an acute infectious disease of virus ætiology, characterized by an abrupt onset with chills, high fever, headache, myalgia, vomiting, abdominal pain, albuminuria, leuchæmoid leucocytosis and hæmorrhagic phenomena increasing with defervescence of the fever; it is said to be transmitted by the mite *Lælaps Jettmari Vitzthum*, the host of the mite and the probable reservoir of the disease being the field rodent *Apodemus agrarius*. It must be borne in mind that, although the pathological facilities in Korea are limited, the foregoing objective findings are so consistent that there is little doubt that this disease can be recognized as a clinical entity.

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# British Medical Association News.

## SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on September 20, 1951, at the Sydney Hospital, Sydney. The meeting took the form of a series of clinical demonstrations by the honorary medical and surgical staff of the hospital.

### Muscular Dystrophy.

DR. E. H. STOKES first showed a female patient, aged thirty-five years, who was suffering from muscular dystrophy. According to the history which she gave on September 6, 1951, she had been in good health up till the age of sixteen years, when she had noticed weakness of the muscles of the back. She stated that she frequently fell down stairs. The weakness gradually increased until she found that she was unable to ascend even a small gradient by the time she was thirty years of age. In addition to the muscles of the back, the muscles of the shoulder girdles and arms were weak, but the muscles of the hands were not affected. She stated that speech was normal, although dysphagia was present. At the age of twenty-seven years she had been troubled by precipitate micturition, which was now her most distressing symptom; but fortunately it was not constantly present. She also suffered from frontal headaches several times a week and experienced difficulty in relaxing in bed owing to the condition of her back muscles. With regard to her previous health, appendicectomy had been performed when she was aged twenty years and tenotomies of the tendons round the ankles a few months later. There was no history suggestive of anterior poliomyelitis, and there were no points of importance in the medical history of her family.

On physical examination of the patient, pronounced weakness of the muscles of the back was noticed. The muscles of the shoulder girdles, the arms and the lower extremities were also affected, but the muscles of the head and neck and the intrinsic muscles of the hands appeared normal in size and power. When she walked her shoulders were projected backwards, a waddling type of gait being produced. There was slight "winging" of the scapulæ. There was no evidence of muscular fasciculation. Sensation was normal, but the biceps, knee and ankle jerks were not elicited. The cranial nerves were normal. She was of a nervous, highly strung disposition, and some of her symptoms such as dysphagia, precipitate micturition and headaches appeared to be of functional origin. X-ray examination of the spine failed to reveal any abnormality. She had received symptomatic treatment and had been instructed in educational exercises and occupational therapy. Splints had been applied at night. The condition had not progressed during the past five years, but she usually improved during the warm weather, and it was reported that the knee jerks had been elicited in the summer months.

Dr. Stokes considered that she was suffering from muscular dystrophy, and said that the slow progress of the condition and the non-involvement of the intrinsic muscles of the hands helped to distinguish it from progressive muscular atrophy.

### Parathyreoid Tumour.

Dr. Stokes's next patient was a woman, aged fifty years, who had consulted him on June 29, 1951, having been referred by Dr. F. T. Willard, of Maclean. She complained of pain in the right buttock and leg of about one year's duration. She had lost considerable weight, and Dr. Willard was of the opinion that her height had decreased over the past few years. On radiological examination of the spine, Dr. H. M. Cutler noted scoliosis, spondylitis and considerable decalcification, but no cyst formation. The history of her previous health was of importance, because she had lost her teeth early in life and in fact she had worn an upper denture since she was fourteen years of age. Her right kidney had been removed at the age of forty-three years on account of a stone, and a calculus had also been removed from the left ureter. The right lobe of the thyreoid gland was enlarged. In view of these findings Dr. Willard suggested that she might be suffering from a parathyreoid tumour. Blood calcium and blood phosphorus estimations by Dr. C. B. Cox gave the following results: the serum calcium content was 14·6 milligrammes per 100 millilitres and the serum phosphorus content 2·7 milligrammes per 100 millilitres. Tests of renal function gave fairly satisfactory results. The patient was then referred to Dr. S. Livingstone Spencer, who removed a tumour the size of a small marble from the posterior aspect of the left upper pole of the thyreoid gland. On microscopic examination it was found that the tumour was an adenoma of the parathyreoid gland. She had made a good recovery since operation. Her weight had increased by a stone and the serum calcium content had remained consistently in the neighbourhood of nine milligrammes per 100 millilitres. It was proposed to watch her progress carefully, as she was still complaining of pain in the right buttock and right leg at the time of the meeting.

### Ankylosing Spondylitis.

DR. A. T. NISBET and DR. F. DUVAL presented a man, aged twenty-four years, who had been first examined in June, 1947, when he gave a history of severe pain in the lower part of the back with increasing stiffness of the spine over a period of about three years. The pain was particularly severe at night. Skiagrams revealed sclerosis of the sacro-iliac joints, typical early changes in ankylosing spondylitis. He had deep X-ray therapy to the lumbar part of his spine and his sacro-iliac joints between June and September, 1947. At the completion of treatment his pain had completely disappeared and movement was unrestricted.

In May, 1951, he noticed some pain in the mid-dorsal section of the spine, and further treatment was given to that area. At the time of the meeting he was well, except that he had occasional pain at night in the mid-dorsal region.

It was pointed out that in retrospect it probably would have been advisable to treat the whole of the spine when the patient was first examined, even though radiological changes were present only in the sacro-iliac joints.

For comparison skiagrams were shown from a case of advanced ankylosing spondylitis with complete rigidity of the lumbar and dorsal sections of the spine; radiotherapy had given some relief of pain. Only osteotomy could correct the deformity.

### Polycythæmia Vera.

Dr. Nisbet and Dr. Duval also presented a man, aged forty-six years, who had been first examined in October, 1943, with a history of headaches, palpitations and severe breathlessness, of two years' duration. The hæmoglobin value of his blood was 17·2 grammes *per centum*, the red cells numbering 5,780,000 per cubic millimetre. From 1943 to 1945 he received deep X-ray therapy to the long bones with some relief of symptoms, but remissions were short. Periodic venesections were also necessary. In 1947 he had to give up work and was granted an invalid pension. In October, 1947, 3·6 millicuries of radioactive phosphorus ($P^{32}$) were given intravenously, and further doses were given of 3·8 millicuries on January 10, 1948, and 4·0 millicuries on November 25, 1948. Improvement occurred slowly and became certain by March, 1949. In July, 1949, he resumed his work as a taxi cab driver, and he had continued at it ever since, feeling better than he had for years. A blood count now gave the following information: the hæmoglobin value was 14·3 grammes *per centum* and the red cells numbered 6,400,000 per cubic millimetre, compared with a hæmoglobin value of 22 grammes *per centum* and a red cell count of 7,500,000 per cubic millimetre before the radiophosphorus was given.

### Carcinoma of the Oral Cavity.

#### *Carcinoma of the Tongue.*

Dr. Nisbet and Dr. Duval also presented three patients who had been treated for carcinoma of the oral cavity.

The first patient, a woman, aged forty-eight years, had been first examined in December, 1948, when two ulcerated areas were present on the right side of the tongue separated by an area of induration. Biopsy revealed a squamous cell carcinoma. A radon needle implant was performed over an area of four by three centimetres, and a tumour dose of 6500*r* was given in seven days. The tongue was healed by January, 1949, and there had been no sign of recurrence since then.

#### *Carcinoma of the Alveolus.*

The second patient, a woman, aged sixty-eight years, had been examined in May, 1950, when she had a raised, hard lump on the lower alveolus in the mid-line. Biopsy showed the lesion to be a squamous cell carcinoma. Treatment was by means of a radon dental mould applied to an area of 2·5 by 1·5 centimetres, a dose of 6500*r* being given in seven days. The area had healed by July, 1950, and had remained healed since.

### *Carcinoma of the Tonsil.*

The third patient, a man, aged seventy-three years, had been examined in March, 1951, when a cauliflower mass three by two centimetres in area was present, arising from the left tonsil and extending onto the soft palate. Biopsy showed it to be a squamous cell carcinoma. Treatment was by deep X rays, an approximate tumour dose of 4500*r* being given over four weeks. The lesion healed rapidly. At the time of the meeting the patient was symptomless and there was no evidence of any residual neoplasm.

### Pharyngeal Pouch.

DR. S. L. SPENCER showed a woman, aged sixty-five years, who had been referred by Dr. Hamilton Kirkland, and who had complained of dysphagia for four years. The patient said that she felt that the food would not go down to the stomach, but that it went into the left side of the neck and then came back. Sometimes the food lodged there and the patient found that she could push it away again with a finger. She had lost about one stone in weight.

Physical examination showed the presence of an adenoma in the right lobe of the thyreoid gland and an indefinite swelling in the lower anterior part of the left posterior triangle. Removal of both the adenoma and the pouch was carried out in one stage on May 11, 1951, the opening in the œsophagus being sutured with silk and fine nylon. The patient's progress since operation had been satisfactory, and she was now able to swallow her food perfectly normally.

Dr. Spencer drew attention to the fact that an occasional elderly patient with dysphagia suffered from this readily curable condition, and expressed the opinion that, with modern aids, a one-stage excision was indicated. In the present case an interesting feature was that the patient said that for many years she had been subject to the effects of conjugal strife, and that tension at mealtimes would upset her so that she would have difficulty in swallowing and would often vomit. Dr. Spencer thought it was possible that the nervous strain had led to some incoordination of deglutition and to a raised intrapharyngeal pressure, which, possibly in addition to some preexisting local weakness, had led to the development of the pulsion diverticulum of the pharynx.

### Intrapelvic Rupture of the Urethra.

Dr. Spencer then showed a wharf labourer, aged thirty-two years, who in 1949 had been run over by a thirty-hundredweight motor-lorry, of which the rear wheel passed over the front of his pelvis. An X-ray film showed fractures of both pubic rami on the left side and separation at the *symphysis pubis*. The left pubic bone was displaced backwards and downwards. A catheter was passed and only some blood and fat globules were recovered.

At operation the bladder was found to be collapsed, with an extraperitoneal tear, while the urethra was ruptured at the apex of the prostate, the latter being rotated backwards with about one and a half inches of separation between the ends of the urethra. Soft rubber catheters were passed from both the external and the internal urinary meatuses and their ends were recovered through the cave of Retzius. The ends were then stitched together, and the resultant elongated tube was used to draw a small catheter of de Pezzer type downwards through the urethra, the expanded end coming to rest against the internal urinary meatus. Traction on the catheter brought about apposition of the ruptured urethra. The tear in the bladder was sutured and drains were left in the cave of Retzius and in the bladder, together with a suture through the expanded end of the de Pezzer catheter to permit the latter to be withdrawn at a later date. The displaced pubic bone was manipulated into position and the patient was treated post-operatively in a pelvic sling. The de Pezzer catheter was removed at the end of two weeks and the patient had since passed urine normally, which he continued to do. He could also walk, and he had been able to return to his previous occupation. About one month after the accident a urethrogram showed a normal outline for the urethra.

Dr. Spencer pointed out the importance of timely recognition and treatment of intrapelvic rupture of the urethra. If the condition was not recognized, or if the necessity for immediate treatment was not appreciated and the patient was managed only by the performance of suprapubic cystostomy, the urethral ends became separated by a barrier of scar tissue, and the patient was almost certainly doomed to a lifelong cystostomy. The method described for correcting the displacement was not difficult and had given good results on a number of occasions. That portion of the urethra showed little tendency to stricture formation, but it was considered advisable to pass sounds at intervals in order to confirm that no narrowing was taking place. Dr. Spencer further drew attention to the fact that such patients usually become impotent for six to twelve months, but said that, in his experience, normal erections had always returned. It was considered of importance that the medical attendant should be aware of that fact, so that he might with confidence assure his patient that his powers would be restored, lest a functional impotence become established.

### Hirschsprung's Disease.

Dr. Spencer also discussed the case of a boy, aged fourteen years, suffering from Hirschsprung's disease, who had been referred by Dr. Alan Young. The parents said that the boy was nursed with difficulty and that during his first few days of life he had had to have meconium washed out of his bowel. Enemas were given about once a week until he was four years old, when an X-ray films was taken showing changes in the large bowel which were regarded as being typical of Hirschsprung's disease. Conservative treatment was continued until the age of seven years, when a neurosurgeon tried "injections into the spine" (possibly spinal anæsthesia) with temporary benefit, and then carried out a sympathectomy without any improvement. In recent years the patient's condition had become worse. Examination with an opaque enema revealed dilatation of the large bowel down to the region of the sigmoid.

Three months prior to the meeting a laparotomy was performed and the transverse colon was brought out through a right rectus incision as a colostomy. While the abdomen was open the level of the transition in the sigmoid colon from dilated to undilated bowel was identified and marked with sutures of black silk. On September 18, 1951, after preparation of the bowel with washouts and instillations of sulphathaladine suspension, a resection of the sigmoid colon and the lower part of the rectum was carried out by the method of Denis Brown. The resected bowel was being examined for evidence of absence of ganglion cells, but the result was not yet to hand. It was proposed to close the colostomy about two or three weeks after the resection.

DR. M. SOFER SCHREIBER said that Swenson's method of resection had been employed at the Royal Alexandra Hospital for Children, and that he thought it had the advantage that immediate examination of frozen sections could be carried out in order to check whether the whole of the abnormal segment of the bowel had been removed.

### Intrathoracic Goitre.

Dr. Spencer's next patient was a woman, aged fifty-two years, who gave a history of having been "shaky, trembly and faint" for six months. She had also noticed palpitations on exertion and some difficulty in breathing and swallowing. She was upset by hot weather, but did not feel the cold. There was no weight loss. Dr. Spencer said that he showed the patient because at the time when she was first examined no swelling could be felt in the neck, although X-ray examination showed the presence of a large mass in the superior mediastinum with the characteristic appearances of an intrathoracic goitre. The cervical portion of the trachea was much displaced to the right, and when a finger was passed over the top of the manubrium and the patient was asked to swallow, the intrathoracic mass could be felt to rise and impinge on the finger. While no originality was claimed for the suggestion. Dr. Spencer thought that an examination of the neck, especially in relation to thyreoid conditions, should always include palpation of the trachea, which not infrequently gave a clue to the presence of a swelling which might not otherwise be obvious. In the present instance the patient had been examined elsewhere, and although the presence of an intrathoracic goitre was suspected from the history, it appeared that the examination made at the time had revealed no abnormality.

DR. C. ENGELS pointed out that when an intrathoracic goitre moved on deglutition, it was sometimes possible to demonstrate a movable level of dulness to percussion at the lower border of the tumour.

### Stricture of Right Hepatic Duct.

Dr. Spencer's last patient was a woman, aged forty-nine years, who had been referred by Dr. C. A. Wiles, and who in 1945 had had her gall-bladder removed at another hospital. She had been well for three months after the operation and had then become jaundiced, and since then her jaundice had recurred at intervals and had been accompanied by pain and rigors. The patient said that three more operations had been carried out at the other hospital, at one of which she understood a rubber tube was introduced into the duct, but no permanent benefit was conferred.

The patient had been examined by Dr. Spencer one year prior to the meeting, when a provisional diagnosis of bile duct stricture was made. In November, 1950, the common bile duct was exposed and explored. The stricture was not found on that occasion, but there was a stone in the common duct, which it was thought explained the patient's symptoms. The stone was removed and the patient remained well for two or three months, but then her pain, shivering and jaundice recurred. On April 17, 1951, the common bile duct was again explored, and on that occasion a passable stricture was discovered which appeared to be in the right hepatic duct. It was not found possible to expose the actual site of the stricture, so the latter was dilated to the size of an 11/14 Lister's bougie, and a long rubber tube with a diameter of about five millimetres was fixed in the duct with one end extending up through the stricture, and the other end led outside the body. It was allowed to remain in position for three months, in the hope that the fibroblastic reaction stimulated by the dilatation would by then have subsided, the tendency to a recurrence of the stricture being thereby minimized. The tube had been removed two or three months previously, and apart from a mild transient attack of jaundice immediately following the removal of the tube, the patient had remained well.

Dr. Spencer emphasized the difficulty presented by patients with strictures in the bile ducts, and pointed out that prevention by careful operative methods was completely superior to any method of cure as yet available.

DR. SELWYN NELSON offered the suggestion on general principles that cortisone might have some use in the management of surgical strictures as a method of reducing fibroblastic reaction. It would, of course, be necessary in surgical cases to take special precautions in regard to wound healing.

### Radiographic Exhibit.

DR. D. G. MAITLAND showed a series of radiographs illustrating the various appearances produced by carcinoma in the stomach and in the colon. Several chest radiographs were also shown, illustrating neurofibroma and bronchogenic carcinoma. Of obstetrical interest was a film showing a post-mature dead *fœtus in utero*, with dense calcification of the placenta. The mother had been taking calcium lactate tablets and a multi-vitamin preparation since the inception of her pregnancy.

### Prolapse of the Uterus.

DR. S. DEVENISH MEARES spoke of prolapse of the uterus with particular reference to prolapse of severe degree, illustrating his remarks with several photographs. Examples of ulceration of the prolapsed tissue were shown. Sometimes ulceration was multiple, on either the cervix or the prolapsed vaginal walls. When the prolapse had been present for many years the epithelium became dry, thick, coarse and rough, with ulceration and sometimes the scars of healed ulcers. All those changes were quickly reversed before operation, by keeping the prolapsed section within the vagina for a week or two, either by means of a pessary or, if a pessary would not remain in place, by rest in bed. The occurrence of carcinoma was exceedingly rare. Dr. Meares then illustrated some difficulties of diagnosis, particularly presented by large cysts of Yaartner's duct and more rarely by large cysts of the posterior vaginal wall. He said that in addition examination must always be made for hernia of the pouch of Douglas. Finally Dr. Devenish Meares showed a photograph of a very large prolapse, which by the weight of the prolapsed tissue had so dragged on the lower end of the urethra as to dilate widely the external meatus.

### Stenosing Tenosynovitis.

DR. R. H. HODGKINSON presented several patients with stenosing tenosynovitis, comparing the results of conservative and operative treatment.

### Tendon Repair.

Dr. Hodgkinson also showed a patient in whom he had performed repair of a ruptured *extensor pollicis longus* tendon following Colles's fracture.

### Morphœa.

DR. A. G. FINLEY first showed a female patient, aged fifty-nine years, who had presented in May, 1951, with an area of thickened skin on her leg, which had been present for six months and was still increasing in size. She was having treatment for "hypertension and nerves" at the time, but was otherwise well. On examination, she had a large irregular patch of circumscribed scleroderma or morphœa on the posterior aspect of the right leg. She was treated with vitamin *B* complex and para-aminobenzoic acid, 50 milligrammes three times a day. At the time of the meeting, four months after treatment was started, the area had not increased in size and had become much softer. Dr. Finley said that the efficiency of para-aminobenzoic acid in the treatment of the condition was difficult to assess because the lesions sometimes resolved spontaneously; hence it was difficult to have an adequate series of control cases.

### Dermatofibrosarcoma Protuberans.

The second patient shown by Dr. Finley was a man, aged fifty-one years, who gave a history of having had "ten inoculations for rabies" into his lower abdominal wall in Shanghai about fifteen years earlier. Within a few years some yellowish patches appeared on the skin at the site. They had not altered very much until approximately a year prior to the meeting, when some small lumps began to appear. As the condition did not worry him, he did not seek medical advice until two weeks previously. He now had a series of yellowish-brown plaques scattered over the lower part of the abdomen and several bluish-coloured tumours, the smallest of which was the size of a pea. The largest was irregular in shape and two inches wide at its longer diameter. There was no attachment to muscle beneath, the whole area being freely movable. Dr. Finley said that clinically the condition was *dermatofibrosarcoma protuberans*, which had been first described by the French dermatologist Darier and was a low-grade fibrosarcoma. It sometimes followed trauma, and the abdominal wall was a common site for it. A biopsy had been performed, but the report was not yet to hand. The condition would be treated by radiotherapy or excision according to the microscopic picture, which would indicate whether the tumours were likely to be radiosensitive.

### Arthroplasty of the Hip Joint.

DR. WARWICK STENING showed three patients who had undergone vitallium cup arthroplasty of the hip joint for disabling osteoarthritis. Two patients were men, aged sixty-seven and sixty-eight years respectively, who had been operated on fifteen and sixteen months before respectively; they had a good range of movement, freedom from pain and good agility. The other patient was a woman, aged forty-eight years, who seven years previously had undergone a Lorenz type osteotomy of the left hip for osteoarthritis with good result, freedom from pain being almost complete, but very little movement being present in this hip joint. Nine months previously vitallium cup arthroplasty was performed to the right hip for osteoarthritis. Dr. Stening said that the patient was shown because, despite the good objective result in the left hip, she was more satisfied with the right hip, even though there was still some pain on weight-bearing, because of recovered movement and strength in that limb compared with the other.

### Hemicolectomy for Diverticulitis.

DR. EDWARD WILSON showed a female patient, aged fifty years, who had been admitted to Sydney Hospital on February 12, 1951, with acute obstruction of the sigmoid colon due to diverticulitis. For the previous five years she had complained of vague lower abdominal pains, and for six months she had complained of "fullness after meals". After the intravenous administration of fluids a laparotomy was performed; this revealed an inflammatory mass obstructing the sigmoid colon. A double-barrelled colostomy opening was constructed. The left side of the colon was isolated but not removed because of her poor general condition and because of a multiplicity of adhesions. On March 20 the colostomy was closed after crushing of the spur. On April 13 left hemicolectomy was performed. On April 28 she was discharged from hospital, apparently cured. Her bowels were then acting normally and there was no abdominal pain. On May 2 she was readmitted to hospital with left femoral thrombosis. She was treated with heparin and lumbar sympathetic blocks. After seven days the pain and swelling subsided, and they had not recurred.

### Anterior Resection of Rectum.

Dr. Wilson next showed a male patient, aged sixty years, who had been admitted to hospital on June 16, 1951, with carcinoma of the rectum. He gave history of urgency of defæcation, diarrhœa, and the passage of blood and mucus *per rectum* for the past twenty months. His general condition was good. On examination of the patient, a fungating tumour one inch in diameter was palpable in the rectum and situated 12 centimetres from the anus. A biopsy showed it to be of a low-grade malignancy. On June 19 a transverse

colostomy opening was established. On July 10 an anterior intraabdominal resection of the rectum was carried out. With the use of a continuous mucosal layer of catgut and an interrupted layer of cotton sutures for the outer layer, an end-to-end anastomosis was performed at the level of the pelvic floor. The rectum was divided 5·5 centimetres below the tumour. Convalescence was uneventful except for slight infection of the abdominal wound. No abscess or fistula formation complicated the post-operative period. Dr. Palmer reported on the excised specimen that there was carcinomatous change in parts of the polypus, but that no infiltration of the pedicle had been found and no metastatic carcinoma in the lymph node sections. On August 14 the patient was discharged to the rectal clinic. The suture line was then healed, but it was palpable anteriorly. He was waiting readmission to hospital for closure of the colostomy.

### Ano-Rectal Fistula.

The next patient shown by Dr. Wilson was a man, aged forty-nine years, who on July 27, 1951, had been admitted to hospital with an ischio-rectal abscess. He gave a history of similar abscesses twenty-five and again two years previously. On July 20 the abscess and the ano-rectal fistula were laid open, including the internal opening, which was situated between the deep part of the external sphincter and the pubo-rectalis. The fistula passed forwards on the left side almost to the pubis and passed across to the right ischio-rectal fossa. A submucous extension was present. On July 27 the first dressing was carried out in the operating theatre under "Pentothal" anæsthesia. Thereafter the wound was irrigated and dressed daily. On August 3 and August 14 the wound was examined under "Pentothal" anæsthesia. On September 11 the patient was discharged to the rectal clinic, the wound having healed. The bowels were open regularly and control was good. Slight mucosal prolapse was present; Dr. Wilson said that that would be overcome as the fibrosis around the anus increased. Such prolapse was to be expected after such widespread removal of the anus and its muscles.

### Reconstruction of Foot.

Dr. Wilson's next patient was a man, aged twenty-two years, who had been admitted to hospital on October 8, 1950, after a motor-cycle accident. That portion of the foot anterior to the talus was attached only by plantar structures and the extensor tendons. It was cold and the circulation in it was poor. After *débridement* the wound was partly closed. A week later the wound was redressed and a further plaster splint was applied under "Pentothal" anæsthesia. There was some sloughing of the lateral aspect of the foot. After another week the slough, which included the fourth and fifth toes and metatarsals, was excised. After a further week the sloughing was more extensive and included the cuboid and lateral and middle cuneiforms; they were then excised. On November 7 the sloughing third toe and the second and third metatarsals were removed. On November 14 the wound was redressed. No further sloughing occurred. On December 5 a skin tube was raised from the abdominal wall. On December 19 a split skin graft was applied to the dorsum and the lateral aspects of the foot. On January 30, 1951, a second-stage tube graft operation was performed. The medial end of the tube was detached from the abdomen and applied to the left wrist. On February 27 the lateral end of the tube was detached from the abdomen and carried down to the foot. Four weeks later the medial end of the tube was detached from the wrist and applied to the foot, the tube not being spread. On May 4 the tube graft was spread on the foot after excision of the temporary split skin graft. Three weeks later the graft was thinned. Thus the whole of the lateral aspect of the sole and lateral border of the foot was replaced by healthy, pliable skin on which weight could be borne. Dr. Wilson said that the patient now had a foot containing the *os calcis*, the talus, the navicular, the medial cuneiform, the first metatarsal, and the first and second toes. The power and movements were good, and he was walking with only a slight limp, which was rapidly decreasing.

### Rectal Prolapse and Incontinence of Fæces.

Dr. Wilson finally showed a female patient, aged forty-seven years, who for the past twenty years had suffered from complete rectal prolapse and rectal incontinence. On examination of the patient, there was no tone in the anal sphincters, and the prolapsed tissue was about five inches long. She had had two unsuccessful operations seventeen and ten years earlier. On August 22, 1950, a rectocele had been repaired.

On October 17 rectosigmoidectomy was performed; about 15 inches of bowel were removed. The site of division was about one inch above the anus. On November 4 she was discharged home with her wound healed. No separation of suture line had occurred. There was no narrowing of the lumen of the bowel, and there was no obvious infection of the perirectal tissues. The control over the bowels had improved. On April 19 she was readmitted to hospital. Thiersch's operation was then performed, silver wire being used. On April 28 she was discharged to a convalescent home. The perianal wounds were then healed. On May 22 she was reexamined; her bowels were then open regularly, and her control over them was greatly improved. When the motions were well formed control was normal.

### Operations on the Biliary Tract.

DR. J. M. YEATES first showed a woman, aged thirty-eight years, who had been awakened at 3 a.m. one morning in August, 1951, by a severe pain on the right side of the abdomen. Shortly afterwards vomiting commenced. The pain persisted during the day and gradually became worse. There had been a similar attack one month previously, though the pain had been more colicky in nature. Examination of the patient revealed tenderness on the right side of the abdomen, most pronounced three inches lateral to the umbilicus. Murphy's sign was absent. In view of all the known facts, acute appendicitis and acute cholecystitis seemed equally likely.

Operation was decided upon and the appendix was inspected first through a gridiron incision. It was obviously innocent, but was removed. A right upper paramedian incision was now made. The gall-bladder was found to be tense and œdematous. A single stone was palpable near the neck of the organ. As the patient's general condition was excellent, cholecystectomy was considered to be the best operation, particularly as signs of inflammation were not excessive. The patient recovered rapidly and was discharged from hospital on the fourteenth day. Detailed examination of the removed gall-bladder showed that a gall-stone one centimetre in diameter was firmly impacted in the cystic duct. Dr. Yeates said that he preferred not to operate on patients with acute cholecystitis. Failure to respond to conservative treatment or doubt about the diagnosis were indications for surgery.

Dr. Yeates's second patient was a woman, aged sixty-two years. In November, 1950, her gall-bladder had been removed for typical cholelithiasis. The common duct appeared normal. On the second post-operative day her condition suddenly deteriorated and much bile flowed from the drainage tube. The abdomen was at once reopened. Some small amount of bile was mopped out. The two silk ligatures on the cystic duct were intact. There was no sign of the origin of the bile. The patient then made excellent progress and was discharged from hospital in two weeks.

She was readmitted to hospital in May, 1951, with a history of severe abdominal pain and vomiting of some months' duration, gradually increasing. Examination revealed that the patient was now emaciated and severely jaundiced. It seemed doubtful whether she would stand an operation. After careful pre-operative treatment laparotomy was performed on May 21, 1951. An encysted collection of bile-stained fluid was found lying between the anterior surface of the stomach and the anterior abdominal wall. The fluid was entirely to the left of the mid-line. There was no bile, and only the most filmy adhesions were present in the region of the common duct. The volume of the fluid was approximately one litre. The common duct was dilated to the size of the duodenum. It was opened, and a crumbling gall-stone measuring two centimetres by one centimetre was removed. The upper and lower reaches of the duct were thoroughly explored, but no more stones were found. Sounds passed with the greatest ease into the duodenum. The duct was sutured completely, without drainage. The patient made a slow but steady recovery, and was discharged from hospital on the thirty-fifth day.

Dr. Yeates said that two questions had to be answered: (i) Where had the bile come from? (ii) Why was it situated so far from the gall-bladder bed?

Dr. Yeates finally showed a woman, aged forty-five years, who had first presented four years previously with recurrent epigastric pain of a colicky nature, associated with flatulence and distaste for fatty food. A Graham's test showed that the gall-bladder contained stones. Cholecystectomy was performed in 1947 and apparently the common duct was not suspected. The pain persisted, and in 1948 recurrent fever and jaundice prompted exploration of the common duct. No stones were found. A size 9/12 sound passed with ease, but

a size 10/13 sound would not pass into the duodenum. The duct was drained with a T tube.

In 1950 the patient was again admitted to hospital because of bouts of fever and malaise. However, no jaundice was present, and the symptoms subsided.

In 1951 malaise, upper abdominal pain, nausea and a muddy complexion brought the patient once more to hospital. Laparotomy was performed in July. The common duct was found to be dilated to the size of the index finger. No stones were palpable. When the duct was opened much thick mud was found, and a soft lump which was in the form of a stone. Probes of all sizes failed to pass into the duodenum. The duodenum was therefore opened, and under direct vision a size 7/10 sound was passed with some difficulty. The duct was then gradually dilated up to the size of a 12/15 sound. The blockage in the duct in this case was obviously due to a condition of fibrosis in the lower part of the duct. A drainage tube was installed in the duct; it was removed on the tenth day and the wound was dry on the twentieth day. The patient's condition was now much improved, but she still complained of pain.

Dr. Yeates said that if further episodes of cholangitis occurred, the best treatment would probably be to anastomose the proximal end of the dilated common duct to a new opening in the duodenum.

### Cranial Surgery.

DR. SCOTT CHARLTON showed a number of patients who had been treated surgically for epilepsy. The conditions involved included cerebral scar, cortical angioma of minute size and not revealed by ordinary methods of investigation (one case), and meningeal cyst secondary to a birth injury (one case). There were two cases in which no macroscopic or microscopic lesion was seen, but in which there were focal signs in the electroencephalogram, and at operation in the electrocorticogram.

Dr. Charlton also showed several patients who had undergone procedures for skull repair, some by means of tantalum prostheses and bone graft. A patient was also shown in whom an immense cranial defect, including the left orbit and the middle fossa, resulted from an operation performed for the removal of a widespread meningioma of the outer third of the left sphenoidal ridge. The patient had recovered, but presented a problem in skull repair, and her case was discussed from that point of view.

### Paraplegia due to Encysted Hæmatoma.

Dr. Charlton finally showed a small boy, suffering from paraplegia due to an encysted extradural hæmatoma of the upper thoracic region. Dr. Charlton said that the patient was shown because of the rarity of the condition, and also because complete spastic paraplegia had been unassociated with any sensory change.

### Spontaneous Hæmatoma of the Rectus Abdominis Muscle Simulating Twisted Ovarian Cyst.

DR. A. A. MOON and DR. G. A. W. JOHNSTON showed a female patient, aged forty-six years, who had three children aged respectively twenty-seven, twenty-five and twenty years; she had had no miscarriages. She had been admitted to hospital from the Board of Health with the provisional diagnosis of ruptured ectopic gestation. The patient had undergone cholecystectomy ten years previously and appendicectomy nine years previously. The present illness had begun with sudden severe pain in the left side of the abdomen forty-eight hours previously; the pain had been constant, unrelieved by any measures, and more severe on movement. Vomiting had been present during the past twenty-four hours. Vaginal hæmorrhage had been present for forty-eight hours, having begun just before the onset of pain. The patient had had no other hæmorrhage *per vaginam* since the menopause two years previously. She had no urinary symptoms and no vaginal discharge, and her bowels were open regularly; her general health was satisfactory.

On examination, the patient was seen to be a middle-aged woman of good colour and not obviously in a state of shock; her pulse rate was 128 per minute and her temperature was normal. She was suffering intense abdominal pain and writhing in bed. Her blood pressure was 200 millimetres of mercury, systolic, and 120 millimetres, diastolic. Bright blood was coming from the vagina. The abdomen was acutely tender, the maximum tenderness being over the lower half on the left side. A tender mass was palpable passing downwards from the left hypochondrium towards the brim of the pelvis; it was regular and smooth, did not appear to move on respiration, and was dull on percussion. Pelvic examination gave negative results, apart from the presence of a little bright blood. No mass or tenderness was present in the fornices.

The patient was thought to have some acute abdominal catastrophe, but the cause was not apparent. A general surgeon, Dr. S. L. Spencer, examined her in consultation and was not sure of the cause. He considered the mass neither splenic nor renal in origin, and in view of the vaginal hæmorrhage and the tenderness low in the abdomen, it was thought that probably the lesion was a twisted ovarian cyst.

An examination under anæsthesia with dilatation and curettage was performed; no pelvic abnormality was found, and the material obtained by curettage appeared normal. Laparotomy was performed. A lower abdominal mid-line incision was made; towards the upper limit of the incision the extraperitoneal tissues were engorged and œdematous. The peritoneum was opened and peritoneal cavity, abdominal viscera and pelvic organs appeared normal. On upward palpation towards the mass, the parietal peritoneum bulged inside the abdomen like a saucer, but was intact. The mass was diagnosed as a hæmatoma of the *rectus abdominis* muscle. A stab wound was made in the loin, and about a cupful and a half of blood clot and dark fluid blood was evacuated. A large drainage tube was inserted into the hæmatoma cavity and the abdominal wound was sutured.

The comment was made that spontaneous hæmatoma of the *rectus abdominis* muscle was a clinical entity, but a rare condition, and the diagnosis was frequently missed. Three cases had been reported from the Beth Israel Hospital over the period 1930 to 1947 (H. Broady). Teske reviewed the literature on the subject in 1946 and analysed 100 cases. In only 17 of the 100 cases was the correct diagnosis made, and in 22 the incorrect diagnosis of twisted ovarian cyst was made. Other pitfalls in diagnosis included appendicitis, irreducible hernia, sarcoma and dermoid of the rectus muscle. The condition was said to be three times more common in women than in men, and it might occur at any age from seventeen to eighty years. Trauma was a frequent cause, and it was usually associated with considerable bodily effort in young men, being especially connected with athletic and military manœuvres. Other ætiological factors were those associated with pregnancy, labour and the puerperium, and degeneration of muscle following debilitating illness. The site of the hæmatoma was most commonly the lower half of the abdomen (in 50% of cases it was in the right lower quadrant of the abdomen). The greater frequency in the lower part of the abdomen was explained on anatomical grounds. Below the level of the *linea semicircularis* where the posterior wall of the rectus sheath ended, the rectus muscle was separated from the peritoneum by the transversalis fascia on which lay the inferior epigastric artery and its anastomoses with the superior epigastric artery. Hence a hæmatoma in the lower half of the muscle was more apt to cause peritoneal irritation. Severe pain was the outstanding symptom, together with the presence of a diffuse, tender, localized mass. Associated vomiting, shock, slight temperature rise and leucocytosis could easily present the picture of an acute abdominal emergency. If a correct diagnosis could be made, rest, sedation and observation might be all that was necessary in the way of treatment.

### Urinary Lithiasis.

DR. L. A. JACOBS presented a demonstration illustrating many aspects of urinary lithiasis. He said that the prevalence of the condition could be gathered from the fact that in 1950, 42% of all major operations in the department of urology at the hospital were directly concerned with its treatment. A short discussion of the ætiology of stone formation was given, and reference was made to the composition of calculi and to their diagnosis. A series of some 25 cases was presented, the histories and X-ray films being shown. The cases covered most of the aspects of calculous disease, and in many unusual features were present. There were examples of gross bilateral disease, cysturia (two cases), giant calculi of the kidney, calculi of the bladder and bladder diverticula, a number of non-opaque calculi, and seven cases of incipient calculous anuria. Two uncommon examples of preputial calculus were shown, one being nearly three inches in diameter.

A pregnant woman was shown who had double kidneys and double ureters. An excretion pyelogram prepared at six months' gestation revealed hydronephrosis of both lower kidneys, the upper kidneys being normal. There was a series of three stones in the lower calyx of the lower right

kidney. *Post partum* the lower right hydronephrosis remained, and heminephrectomy was performed. The question was debated why the "physiological" hydronephrosis of pregnancy affected only the two lower kidneys.

The relative radiological translucency of stones was discussed and an explanatory skiagram was shown. It was pointed out that the translucency of stones depended on the atomic weights of the various elements in their composition. For example, the atomic weight of hydrogen was 1, that of carbon 6, that of nitrogen 7, that of oxygen 8, that of phosphorus 15 and that of calcium 20. Thus uric acid, $C_5N_4H_4O_3$, was usually radiotransparent, while stones containing calcium and phosphorus were usually opaque. Many stones of various types and kidneys were presented. There was also a model bladder containing stones and a cystoscope.

## Out of the Past.

***In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.***

### MEDICAL REFORM.

[To the Editor of the *Australian Medical Journal.*]

Heidelberg, 4th Aug., 1856.

Sir,

I am more than pleased to see, from the "Medical Journal", that our profession is about to do more than write or speak concerning *Medical Reform.* I really do not think that any legally qualified medical practitioner will be found in Victoria to oppose any measure having this end in view, unless some interested, unworthy party whom no gentlemen would wish to meet or associate with, or even think it worth his pains to kick out of the way. I am the more sanguine of seeing enacted a measure of Medical Reform on account of the absence of all chartered or vested rights. I cordially agree with you, Sir, in all you have written upon this subject with the exception of Druggists being allowed to prescribe over the counter. If *Druggists will prescribe let them qualify,* for should you concede this privilege to them, every *Quack* in the colony would not only become a Druggist, but your Bill would resemble an otherwise healthy child, with an *Equinovarus* on the one foot and a *valgus* on the other: which would in all probability take years to rectify, even although the best surgical skill and mechanical contrivances were brought to bear. I would, however, rather have a bill with the *swinging shanks,* than that we should remain in our present anomalous position. I wish, if eligible, to become a member of your Medical Society, but not being often in Melbourne, you perhaps will let me know how I have to proceed and I remain

Dear Sir yours very truly

ALEXANDER MCGREGOR.

## Obituary.

### WILFRID WANOSTROCHT GIBLIN.

WE are indebted to Sir Victor Hurley for the following appreciation of the late Dr. Wilfrid Wanostrocht Giblin.

The recent death of Wilfrid Wanostrocht Giblin, C.B., V.D, has removed one of the oldest practising members of the profession in Tasmania. He was in his seventy-ninth year, and was engaged in active professional work until shortly before his death. On his last day of practice, three weeks before his last illness, he saw eighteen patients—"rather a big day for me these days".

After his earlier education at the Hutchins School, Hobart, Wilfrid Giblin proceeded to London and entered as a student at Saint Bartholomew's Hospital, London. After qualifying M.R.C.S., L.R.C.P. in 1895, he returned to Hobart to take over the practice of his elder brother, Dr. Edward Giblin, who died suddenly. He joined the honorary medical staff of the Hobart Hospital in 1903, and resigned along with the other members of the staff in 1919. During the many years he practised in Hobart, Giblin took an active part in medical affairs. He was President of the Tasmanian Branch of the British Medical Association in 1919, and was a member of the Federal Committee, as it then was, from 1920 to 1923. He was a member of the Australasian Medical Publishing Company, Limited, from 1919 to 1947. He became a Fellow of the Royal Australasian College of Surgeons in 1928.

Giblin's qualities were well appreciated by all those who knew him in Tasmania, but it was through his outstanding service in the first World War that he became more widely known to a large number of medical officers from the other States of the Commonwealth. From his earliest days Giblin took a keen interest in military affairs. With his erect figure and military bearing and poise, he looked the part

of a thoroughly efficient officer. Standing well over six feet, he was an outstanding figure in any company. At the outbreak of war in 1914 he was the Principal Medical Officer of the Sixth Military District (Tasmania) and was appointed to command the First Australian Casualty Clearing Hospital, which embarked with other Australian hospital units towards the end of 1914 on the *S.S. Kyarra.* Early in the Gallipoli campaign the unit was disembarked at Anzac, and continued work there until the evacuation. Many difficulties were encountered, but under Giblin's leadership these were surmounted. Accommodation for personnel and patients was provided in dugouts in the cliff face and in improvised shelters on the beach, which were under intermittent enemy artillery fire. Evacuation of patients to the hospital ships anchored off shore was hazardous, and usually carried out at night under cover of darkness. The late John Gordon, of Melbourne, and John Corbin, of Adelaide, also rendered splendid service in caring for the large numbers of Australian sick and wounded who passed through the unit. When the Australian Imperial Force was transferred to the Western Front in 1916 a headquarters was established in Horseferry Road, London. Sir Neville Howse, who had in the meantime been appointed Director of Medical Services, selected Giblin as his Deputy Director of Medical Services, and he occupied this post until he returned to Australia towards the end of the war. He was mentioned twice in dispatches, and awarded the C.B. for his services.

After his return he continued to conduct a large practice in Hobart and to be actively interested in medical affairs. He was a keen ornithologist and fly fisherman, and spent most of his holidays in these pursuits.

[1] From the original in the Mitchell Library, Sydney.

He had two sons and two daughters. One of his sons, Mr. Thomas Giblin, of Hobart, is one of the present Tasmanian representatives on the Federal Council.

Sir Henry Newland writes: It is one of the great advantages of attendance at the Australasian Medical Congresses that they furnish welcome opportunities for members to form durable links with those who dwell in other States. It was in this wise that my long friendship with the late W. W. Giblin was conceived, and from time to time refreshed, for he was a "good congress man". In December, 1914, the year of the outbreak of the first World War, we embarked on the *Kyarra*, a transport whose ultimate fate neither of us regretted—"God rest her sunken timbers". Giblin was colonel commanding the First Australian Casualty Clearing Station. I was a major in the First Australian Stationary Hospital. Life aboard ship linked us in closer friendship. Although my unit occupied a site adjoining that of the First Australian Casualty Clearing Station during the last few weeks of the Anzac landing on Gallipoli, Giblin and I did not meet again until I reported when he was Acting Director of Medical Services at Horseferry Road, London. Prior to the war he was one of those all too few medical practitioners who were ardently interested in the Australian Army Medical Service and its efficiency. His seniority and competency led to the high position he occupied at the Australian Military Headquarters. Of a tall and graceful figure, his uniform became him well. The penetrating gaze of his keen blue eyes was impressive. His delightful smile associated with a pleasant voice was captivating. He will be much missed by those who, like myself, derived much pleasure from Giblin's genial friendship.

## GLAUD REAY WALKER.

WE regret to announce the death of Dr. Glaud Reay Walker, which occurred on November 28, 1951, at Ashfield, New South Wales.

## BRUCE MAITLAND CARRUTHERS.

WE regret to announce the death of Dr. Bruce Maitland Carruthers, which occurred on November 29, 1951, at Hobart, Tasmania.

# Correspondence.

## SECURITY AND FREEDOM.

SIR: The theme of your editorial of November 17, 1951, applies to our present paranoid world politics. Sovereign States, not without cause, accuse each other of limiting freedom. At the same time they "aim at security", which Professor Macmurray, as you say, thinks is "multiplying the occasions of fear and magnifying our need for security". President Truman and Generalissimo Stalin have proposed disarmament gestures, each providing that his own trump card shall be kept till last, the other fellow's being discarded first! Your conclusion that "security is . . . to be won chiefly by efforts to secure the future of other people" and the need for a positive, not negative, approach for this, points up the well-proved futility of disarmament plans.

Our state of siege known as the "cold war", like many others before it, is like a chess game where freedoms are "pawned" by both sides, where might comes before democracy in more and more decisions until one side reaches a despair deeper than they expect from the dictatorship of the enemy. Then they clutch at this tyranny, not because they think surrender will "free" them from anything, but, to mix my similes, like the drowning man at his proverbial straw. To put democracy before power politics, co-prosperity schemes before armament blocs, justice and neighbourliness before blind prejudice, we must realize with Macmurray that "we can increase our freedom by limiting our desires without any change in the means of action at our disposal".

## DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED NOVEMBER 17, 1951.[1]

| Disease. | New South Wales. | Victoria. | Queensland. | South Australia. | Western Australia. | Tasmania. | Northern Territory. | Australian Capital Territory. | Australia. |
|---|---|---|---|---|---|---|---|---|---|
| Acute Rheumatism | .. | .. | .. | .. | .. | .. | 1 | 1 | 2 |
| Amœbiasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Ancylostomiasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Anthrax | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Bilharziasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Brucellosis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Cholera | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Chorea (St. Vitus) | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Dengue | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Diarrhœa (Infantile) | .. | .. | 9(9) | .. | .. | .. | 5 | .. | 14 |
| Diphtheria | 4(3) | 2 | .. | 1(1) | 2(2) | .. | .. | .. | 9 |
| Dysentery (Bacillary) | .. | 2(2) | 2(2) | .. | .. | .. | 1 | .. | 5 |
| Encephalitis | .. | 1 | 1 | .. | .. | .. | .. | .. | 2 |
| Filariasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Homologous Serum Jaundice | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Hydatid | .. | 1 | .. | .. | .. | .. | .. | .. | 1 |
| Infective Hepatitis | .. | .. | .. | .. | 6(5) | .. | .. | .. | 6 |
| Lead Poisoning | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Leprosy | .. | .. | .. | .. | 3 | .. | 2 | .. | 5 |
| Leptospirosis | .. | .. | 5(1) | .. | .. | .. | .. | .. | 5 |
| Malaria | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Meningococcal Infection | 2(1) | .. | .. | .. | .. | .. | .. | .. | 2 |
| Ophthalmia | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Ornithosis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Paratyphoid | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Plague | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Poliomyelitis | 8(4) | 1 | 8(2) | 37(22) | 2(1) | .. | .. | .. | 56 |
| Puerperal Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Rubella | .. | 13(8) | .. | .. | .. | .. | .. | .. | 13 |
| Salmonella Infection | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Scarlet Fever | 19(9) | 13(8) | 1(1) | 4(2) | 1(1) | 2 | .. | .. | 40 |
| Smallpox | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Tetanus | .. | .. | 1 | .. | .. | .. | .. | .. | 1 |
| Trachoma | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Trichinosis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Tuberculosis | 67(53) | 3(1) | 23(23) | 8(6) | 7(6) | 1 | 1 | .. | 115 |
| Typhoid Fever | 1(1) | .. | .. | .. | .. | .. | .. | .. | 1 |
| Typhus (Flea-, Mite- and Tick-borne) | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Typhus (Louse-borne) | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Yellow Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |

[1] Figures in parentheses are those for the metropolitan area.

Let us agree to wrest from national governments certain rights: the right to judge international disputes and the right to wage war. Let us give a mandate to a democratic world body to make laws, tax us, set up courts, and police their authority to keep the peace and to limit national militias to internal policing needs. Until we do this, UNO will keep the peace about as well as a schoolboy in a bull-ring. To those who accept Bernard Shaw's challenge (that liberty means responsibility and that that is why most men dread it), I appeal to them, with you, to "choose freedom" and, in Macmurray's words, "triumph over fear". They can make their convictions vocal, if not forceful, by joining the World Movement for World Federal Government. Anyone who cares to inquire from me or from Box 3904TT, G.P.O., Sydney, will, I think, be agreeably amazed to learn what concrete progress this body has made, especially overseas, in a few short years, and how many illustrious names are among its leaders everywhere.

The ideal practice of medicine is not the only responsibility which goes with our freedoms. "To believe in freedom . . . is to believe in setting other people free." In the spread of a movement from man to man, already pointing the way to establishing the peace justly, and toward earning for democracy the respect of all freedom-lovers, lies our one sane hope of dissolving, ultimately, all suicidal "iron curtains".

Yours, etc.,

Mental Hospital,
Gladesville,
New South Wales.
November 17, 1951.

DOUGLAS N. EVERINGHAM.

# Australian Medical Board Proceedings.

## NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1945, as duly qualified medical practitioners:

Conlon, Basil Michael Joseph, M.B., B.S., 1940 (Univ. Melbourne), 439 Liverpool Street, Darlinghurst.

Fisk, Graham Bristow, M.B., B.S., 1946 (Univ. Adelaide), District Hospital, Broken Hill.

McCready, Ian Anthony Jobson, M.R.C.S. (England), L.R.C.P. (London), 1942, c.o. Dr. J. K. Harbison, Murwillumbah.

Rodriguez, Roshun, B.M., B.Ch., 1943 (Univ. Oxford), F.R.C.S. (England), 1949, 6 Priory Road, Waverton.

Tow, Peter Macdonald, M.B., B.S., 1944 (Univ. London), 44 Beaumont Street, Rose Bay.

Vear, Cedric Steadman, M.B., B.S., 1947 (Univ. Melbourne), Denison Street, Finley.

Weiner, Nathan, M.B., Ch.B., 1947 (Univ. Glasgow), 86 Drumalbyn Road, Bellevue Hill.

The following additional qualifications have been registered:

Bauer, Gaston Egon (M.B., B.S., 1946, Univ. Sydney), 115 Shirley Road, Roseville, M.R.C.P. (London), 1951.

Robinson, Clive Frederic (M.B., 1915, Univ. Sydney), 143 Macquarie Street, Sydney, Ch.M., 1951 (Univ. Sydney).

Selby, George (M.B., B.S., 1946, Univ. Sydney), 1361 Pacific Highway, Turramurra, M.R.C.P. (London), 1950, M.R.C.P. (Edinburgh), 1951.

## TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Act*, 1918, as duly qualified medical practitioners:

Hunt, John Gordon, M.B., B.S., 1943 (Univ. London), M.M.S.A. (London), 1946, Claremont.

Poustie, Clyde Thomas, M.B., B.S., 1947 (Univ. Melbourne), c.o. Repatriation Department.

Pitt, Peter Charles, M.B., B.S., 1951 (Univ. Melbourne), Royal Hobart Hospital, Hobart.

The following additional qualification has been registered:

Beattie, J. G. H., M.R.A.C.P., 1948.

# Notice.

## THE ARTHUR WILSON MEMORIAL FUND.

THE following donations have been received for the Arthur Wilson Memorial Fund and are acknowledged with thanks. The fund will be devoted to research into problems of childbirth. Donations may be sent to Dr. C. K. Churches, honorary treasurer, 122 Flinders Street, Melbourne, C.1, and will be acknowledged in this journal. Previously acknowledged £2286 2s., Dr. W. Flynn £25, Dr. W. G. MacGregor £5, Dr. Alfred P. Derham £1 1s. Total £2317 3s.

# Diary for the Month.

DEC. 18.—New South Wales Branch, B.M.A.: Ethics Committee.
DEC. 20.—Victorian Branch, B.M.A.: Executive Committee.
DEC. 21.—Queensland Branch, B.M.A.: Council Meeting.

# Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

*New South Wales Branch* (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

*Victorian Branch* (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

*Queensland Branch* (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

*South Australian Branch* (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

*Western Australian Branch* (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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